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<input type="checkbox"/>	L4	(produc\$ pr isolat\$ or identif\$) near3 l1	108
<input type="checkbox"/>	L3	l1 same (reporter DNA or reporter gene)	20
<input type="checkbox"/>	L2	L1 same (ikaros and scl)	3
<input type="checkbox"/>	L1	hematopoietic stem cell	4856

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FILE 'HOME' ENTERED AT 16:01:52 ON 12 FEB 2004

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=> s Ikaros and SCL
L1 12 IKAROS AND SCL

=> s I1 and hematopo? stem cell?
L2 5 L1 AND HEMATOPO? STEM CELL?

=> dup rem I2

PROCESSING COMPLETED FOR L2
L3 5 DUP REM L2 (0 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 5 ANSWERS - CONTINUE? Y/(N):y

L3 ANSWER 1 OF 5 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

AN 2003:348393 BIOSIS
DN PREV200300348393

TI Self-renewal and differentiation of ***hematopoietic*** ***stem***
cells : A molecular approach (A review).

AU Uher, F. [Reprint Author]; Hajdu, Melinda [Reprint Author]; Vas, Virag [Reprint Author]

CS Stem Cell Biology, National Medical Center, Dioszegi ut 64, Budapest, Hungary

SO Acta Microbiologica et Immunologica Hungarica, (2003) Vol. 50, No. 1, pp. 3-21. print.

ISSN: 1217-8950 (ISSN print).

DT Article

General Review; (Literature Review)

LA English

ED Entered STN: 30 Jul 2003

Last Updated on STN: 30 Jul 2003

AB Two characteristics define a ***hematopoietic*** ***stem***
cell : the ability to differentiate into all hematopoietic lineages, and the ability to maintain hematopoiesis over a life span by a self-renewal process. The mechanisms that regulate the fate of blood-forming cells in vivo, however, are poorly understood. Despite the ability to culture hematopoietic progenitor cells (committed to particular lineages), in vitro culture of self-renewing multipotent stem cells has not yet been achieved. What is clear that both intrinsic and extrinsic signals regulate ***hematopoietic*** ***stem*** ***cell*** fate and some of these signals have now been identified, which will be highlighted in this review.

L3 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:637808 CAPLUS

DN 137:152031

TI Stem cell self-renewal and lineage commitment

IN Chan, Chang-zheng; Lodish, Harvey F.

PA Whithead Institute for Biomedical Research, USA

SO PCT Int. Appl., 36 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2002084756	A2	20020822	WO 2002-US4459	20020215
WO 2002084756	C2	20021114		
WO 2002084756	A3	20030109		
WO 2002084756	C1	20030410		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, NI, TD, TG

US 2002168660 A1 20021114 US 2002-77178 20020215

PRAI US 2001-269060P P 20010215

AB Methods of marking pluripotent cells, such as stem cells, particularly ***hematopoietic*** ***stem*** ***cells*** ; methods of detecting/identifying, enriching, selecting and monitoring pluripotent cells (stem cells); DNA constructs useful in the methods; stem cells, such as ***hematopoietic*** ***stem*** ***cells*** , identified by the method; as well as lineage-specific cells identified by the method; and uses for the cells are subjects of this invention. The cells are marked by targeting reporter genes into loci that are functionally specific and important for ***hematopoietic*** ***stem*** ***cell*** activity (e.g., self-renewal or lineage commitment). Combinations of targeted markers are used to provide phys. and functional identities for the cells. Two loci, stem cell leukemia (***SCL***) and ***Ikaros*** , were targeted using HuCD4/RES/puro and .beta.neo(lacZneo) reporter cassettes, resp.

L3 ANSWER 3 OF 5 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN

AN 2001143930 EMBASE

TI FLRF, a novel evolutionarily conserved RING finger gene, is differentially expressed in mouse fetal and adult ***hematopoietic*** ***stem*** ***cells*** and progenitors.

AU Abdullah J.M.; Li X.; Nachtman R.G.; Jurecic R.

CS R. Jurecic, Department of Microbiology, Univ. of Miami School of Medicine, 1600 NW 10th Avenue, Miami, FL 33136, United States.

rjurecic@med.miami.edu

SO Blood Cells, Molecules, and Diseases, (2001) 27/1 (320-333).

Refs: 43

ISSN: 1079-9796 CODEN: BCMDFX

CY United States
DT Journal; Article
FS 022 Human Genetics
025 Hematology
029 Clinical Biochemistry

LA English
SL English

AB Through differential screening of mouse ***hematopoietic***

stem ***cell*** (HSC) and progenitor subtracted cDNA libraries we have identified a HSC-specific transcript that represents a novel RING finger gene, named FLRF (fetal liver ring finger). FLRF represent a novel evolutionarily highly conserved RING finger gene, present in *Drosophila*, zebrafish, *Xenopus*, mouse, and humans. Full-length cDNA clones for mouse and human gene encode an identical protein of 317 amino acids with a C(3)HC(4) RING finger domain at the amino terminus. During embryonic hematopoiesis FLRF is abundantly transcribed in mouse fetal liver HSC (Sca-1(+)c-kit(+)AA4.1(+)Lin(-) cells), but is not expressed in progenitors (AA4.1(-)). In adult mice FLRF is not transcribed in a highly enriched population of bone marrow HSC (Rh-123(low)Sca-1(+)c-kit(+)Lin(-) cells). Its expression is upregulated in a more heterogeneous population of bone marrow HSC (Lin(-)Sca-1(+) cells), downregulated as they differentiate into progenitors (Lin(-)Sca-1(-) cells), and upregulated as progenitors differentiate into mature lymphoid and myeloid cell types. The human FLRF gene that spans a region of at least 12 kb and consists of eight exons was localized to chromosome 12q13, a region with frequent chromosome aberrations associated with multiple cases of acute myeloid leukemia and non-Hodgkin's lymphoma. The analysis of the genomic sequence upstream of the first exon in the mouse and human FLRF gene has revealed that both putative promoters contain multiple putative binding sites for several hematopoietic (GATA-1, GATA-2, GATA-3, ***IkaroS***, ***SCL*** /Tal-1, AML1, MZF-1, and Lmo2) and other transcription factors, suggesting that mouse and human FLRF expression could be regulated in a developmental and cell-specific manner during hematopoiesis. Evolutionary conservation and differential expression in fetal and adult HSC and progenitors suggest that the FLRF gene could play an important role in HSC/progenitor cell lineage commitment and differentiation and could be involved in the etiology of hematological malignancies. .COPYRG. 2001 Academic Press.

L3 ANSWER 4 OF 5 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN

AN 1999005935 EMBASE

TI Lymphocyte development in fish and amphibians.

AU Hansen J.D.; Zapata A.G.

CS J.D. Hansen, Basel Institute for Immunology, 487 Grenzacherstrasse, CH-4005 Basel, Switzerland. hansen@bii.ch

SO Immunological Reviews, (1998) 166/ (199-220).

Refs: 159

ISSN: 0105-2896 CODEN: IMRED2

CY Denmark

DT Journal; General Review

FS 025 Hematology

026 Immunology, Serology and Transplantation

LA English

SL English

AB Recently, molecular markers such as recombination activating genes (RAG),

terminal deoxynucleotidyl transferase (TdT), stem cell leukemia hematopoietic transcription factor (***SCL***), ***IkaroS*** and gata-binding protein (Gata)-family members have been isolated and characterized from key lower vertebrates, adding to our growing knowledge of lymphopoiesis in ectotherms. In all gnathostomes there appear to be two main embryonic locations derived from the early mesoderm, both intra- and extraembryonic, which contribute to primitive and definitive hematopoiesis based upon their differential expression of ***SCL***, Gata-1, Gata-2 and myeloblastosis oncogene (c-myl). In teleosts, a unique intraembryonic location for ***hematopoietic*** ***stem*** ***cells*** termed the intermediate cell mass (ICM) of Oellacher appears to be responsible for primitive or definitive hematopoiesis depending upon the species being investigated. In *Xenopus*, elegant grafting studies in combination with specific molecular markers has led to a better definition of the roles that ventral blood islands and dorsal lateral plate play in amphibian hematopoiesis, that of primitive and definitive lymphopoiesis. After the early embryonic contribution to hematopoiesis, specialized tissues must assume the role of providing the proper microenvironment for T and B-lymphocyte development from progenitor stem cells. In all gnathostomes, the thymus is the major site for T-cell maturation as evidenced by strong expression of developmental markers such as ***IkaroS***, Rag and TdT plus expression of T-cell specific markers such as T-cell receptor, beta, and lck. In this respect, several zebrafish mutants have provided new insights on the development of the thymopoietic environment. On the other hand, the sites for B-cell lymphopoiesis are less clear among the lower vertebrates. In elasmobranchs, the spleen, Leydig's organ and the spiral valve may all contribute to B-cell development, although pre-B cells have yet to be fully addressed in fish. In teleosts, the kidney is undeniably the major source of B-cell development based upon functional, cellular and molecular indices. Amphibians appear to use several different sites (spleen, bone marrow and/or kidney) depending upon the species in question.

L3 ANSWER 5 OF 5 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN

AN 95365788 EMBASE

DN 1995365788

TI Hematopoiesis: How does it happen?.

AU Orkin S.H.

CS Division of Hematology and Oncology, Children's Hospital, 300 Longwood Avenue, Boston, MA 02115, United States

SO Current Opinion in Cell Biology, (1995) 7/6 (870-877).

ISSN: 0955-0674 CODEN: COCBE3

CY United Kingdom

DT Journal; General Review

FS 021 Developmental Biology and Teratology

025 Hematology

029 Clinical Biochemistry

LA English

SL English

AB Hematopoiesis entails the generation of stem cells, the proliferation and maintenance of multipotential progenitors, and lineage commitment and maturation. During the past year, critical components of these steps have been defined. Notable are gene-targeting experiments in mice in which one or more hematopoietic lineages have been shown to be ablated upon inactivation of several nuclear regulatory proteins (GATA-2, Tal-1/ ***SCL***, Rbtl2/LMO2, PU.1, ***IkaroS***, E2A, and Pax-5), and experiments that establish GATA-1 as a factor capable of programming at least three lineages (erythroid, thrombocytic, and eosinophilic) from a transformed avian progenitor cell.

=> d his

(FILE 'HOME' ENTERED AT 16:01:52 ON 12 FEB 2004)

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 16:02:00 ON 12 FEB 2004

L1 12 S IKAROS AND SCL
L2 5 S L1 AND HEMATOPOI? STEM CELL?
L3 5 DUP REM L2 (0 DUPLICATES REMOVED)

=> s hematopoi? stem cell?

L4 29844 HEMATOPOI? STEM CELL?

=> s l4 (5a) (isolat? or identif? or sort?)

L5 529 L4 (5A) (ISOLAT? OR IDENTIF? OR SORT?)

=> s l5 and reporter and genomic loc?

L6 0 L5 AND REPORTER AND GENOMIC LOC?

=> s l5 and reporter

L7 4 L5 AND REPORTER

=> s l5 and marker

L8 67 L5 AND MARKER

=> s l5 and marker?

L9 116 L5 AND MARKER?

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PROCESSING COMPLETED FOR L7

L10 4 DUP REM L7 (0 DUPLICATES REMOVED)

=> d bib abs 1-

YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y(N):y

L10 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:931540 CAPLUS

DN 140:719

TI Method of identifying pancreatic ductal carcinoma (PDC)-specific gene from pancreatic ductal cells, and using thereof for drug screening and drug testing

IN Mano, Hiroyuki

PA Fujisawa Pharmaceutical Co., Ltd., Japan

SO PCT Int. Appl., 86 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO	2003097879	A2	20031127	WO	2003-JP6398	20030522
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MV, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, VU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM							
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG							

PRAI US 2002-382022P P 20020522

AB We purified ductal epithelial cells, by the use of affinity column for MUC1 (a common surface marker for pancreatic ductal cells), from the pancreatic juice isolated from healthy individuals as well as those with

PDC. Microarray anal. among these background-matched samples of 3456 human genes has identified a no. of carcinoma-specific genes. In particular, disclosed are eight PDC-specific genes including AC133 (five-transmembrane hematopoietic stem cell antigen), CEACAM7 (carcinoembryonic antigen-related cell adhesion mol. 7), SOD2 (superoxide dismutase 2), CDKN1C (cyclin-dependent kinase inhibitor 1C p57, Kip2), HSP105 (heat shock 105kD protein), IGFBP1 (insulin-like growth factor binding protein 1), UBE3A (ubiquitin protein ligase E3A), and CAPN2 (calpain, large polypeptide 2). Cancer-specific expression of these genes was further confirmed by a quant. real-time PCR method. Our microarray anal. with purified pancreatic ductal cells has paved a novel way to develop a sensitive detection method for PDC by the use of pancreatic juice which is routinely obtained in clin. conditions. A pancreatic ductal carcinoma-specific gene can be efficiently identified by utilizing this method, and thereby, it is possible to provide a target that is important for developing a drug for the test of pancreatic ductal carcinoma and the treatment or prevention of pancreatic ductal carcinoma.

L10 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS ON STN

AN 2002:637808 CAPLUS

DN 137:152031

TI Stem cell self-renewal and lineage commitment

IN Chan, Chang-zheng; Lodish, Harvey F.

PA Whithead Institute for Biomedical Research, USA

SO PCT Int. Appl., 36 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002064756	A2	20020822	WO 2002-US4459	20020215
WO 2002064756	C2	20021114		
WO 2002064756	A3	20030109		
WO 2002064756	C1	20030410		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002168660	A1	20021114	US 2002-77178	20020215
PRAI US 2001-269060P	P	20010215		
AB Methods of marking pluripotent cells, such as stem cells, particularly ***hematopoietic***, ***stem***, ***cells***; methods of detecting/ ***identifying***, enriching, selecting and monitoring pluripotent cells (stem cells); DNA constructs useful in the methods; stem cells, such as ***hematopoietic***, ***stem***, ***cells***, ***identified*** by the method; as well as lineage-specific cells identified by the method; and uses for the cells are subjects of this invention. The cells are marked by targeting ***reporter*** genes into loci that are functionally specific and important for hematopoietic stem cell activity (e.g., self-renewal or lineage commitment). Combinations of targeted markers are used to provide phys. and functional identities for the cells. Two loci, stem cell leukemia (SCL) and Ikaros, were targeted using HuCD4/RES/puro and .beta.neo(lacZneo) ***reporter*** cassettes, resp.				

L10 ANSWER 3 OF 4 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN

AN 2002364233 EMBASE

TI Erythroid expansion mediated by the Gfi-1B zinc finger protein: Role in normal hematopoiesis.

AU Osawa M.; Yamaguchi T.; Nakamura Y.; Kaneko S.; Onodera M.; Sawada K. I.;

Jegalian A.; Wu H.; Nakauchi H.; Iwama A.

CS A. Iwama, Laboratory of Stem Cell Therapy, Center for Experimental Medicine, University of Tokyo, 4-6-1 Shirokanedai, Minato-ku, Tokyo 108-8639, Japan. aiwama@ims.u-tokyo.ac.jp

SO Blood, (15 Oct 2002) 100/8 (2769-2777).

Refs: 31

ISSN: 0006-4971 CODEN: BLOOAW

CY United States

DT Journal; Article

FS 025 Hematology

029 Clinical Biochemistry

LA English

SL English

AB In the search for genes expressed in ***hematopoietic***, ***stem***, ***cells***, we ***identified*** that the expression of Gfi-1B (growth factor independence-1B) is highly restricted to hematopoietic stem cells, erythroblasts, and megakaryocytes. Gfi-1 and Gfi-1B are zinc finger proteins that share highly conserved SNAG and 6 zinc finger domains. Gfi-1 has been characterized as an oncogene involved in lymphoid malignancies in mice. In contrast, role of Gfi-1B in hematopoiesis has not been well characterized. In this study, we analyzed its function in human hematopoiesis. Enforced expression of Gfi-1B in human CD34(+) hematopoietic progenitors induced a drastic expansion of erythroblasts in

an erythropoietin-independent manner. Expression of Gfi-1B did not promote erythroid commitment, but enhanced proliferation of immature erythroblasts. Erythroblasts expanded by exogenous Gfi-1B, however, failed to differentiate beyond proerythroblast stage and showed massive apoptosis. These biologic effects of Gfi-1B were mediated through its zinc finger domain, but not by the SNAG or non-zinc finger domain. Proliferation of erythroblasts was associated with sustained expression of GATA-2 but not of GATA-1, indicating a potential link between Gfi-1B and GATA family regulators. Importantly, the function of Gfi-1B to modulate transcription was dependent on promoter context. In addition, activation of transcription of an artificial promoter was mediated through its zinc finger domain. These findings establish Gfi-1B as a novel erythroid regulator and reveal its specific involvement in the regulation of erythroid cell growth through modulating erythroid-specific gene expression. .COPYRG. 2002 by The American Society of Hematology.

L10 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS ON STN

AN 2002:206353 CAPLUS

DN 137:30975

TI Expression of the Ly-6A (Sca-1) lacZ transgene in mouse hematopoietic stem cells and embryos

AU Ma, Xiaoqian; De Bruijn, Marella; Robin, Catherine; Peeters, Marian; Kong-A-San, John; De Wit, Ton; Snoijs, Corne; Dzierzak, Elaine

CS Department of Cell Biology and Genetics, Erasmus University, Rotterdam, 3000 DR, Neth.

SO British Journal of Haematology (2002), 116(2), 401-408

CODEN: BJHEAL; ISSN: 0007-1048

PB Blackwell Publishing Ltd.

DT Journal

LA English

AB The Sca-1 surface glycoprotein is used routinely as a marker for hematopoietic stem cell enrichment. Two allelic genes, Ly-6A and Ly-6E, encode this marker and appear to be differentially regulated in hematopoietic cells and hematopoietic stem cells. The Sca-1 protein has been shown to be expressed at a greater frequency in these cells from Ly-6A strains of mice. To study the specific expression pattern and hematopoietic regulation of the Ly-6A gene, we constructed a 14 kb cassette from a genomic Ly-6A fragment, inserted a lacZ ***reporter*** gene and created transgenic mice. We found that the Ly-6A lacZ transgene was expressed in the hematopoietic tissues and predominantly in the T-lymphoid lineage. Some expression was also found in the B-lymphoid and myeloid lineages. We demonstrated functional ***hematopoietic***, ***stem***, ***cell*** enrichment by ***sorting*** for .beta.-galactosidase-expressing cells from the bone marrow. In addn., we found an interesting embryonic expression pattern in the AGM region, the site of the first hematopoietic stem cell generation. Surprisingly, when compared with data from Ly-6E lacZ transgenic mice, our results suggest that the Ly-6A cassette does not improve lacZ marker gene expression in hematopoietic cells.

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD

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(FILE 'HOME' ENTERED AT 16:01:52 ON 12 FEB 2004)

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 16:02:00 ON 12 FEB 2004

L1	12 S IKAROS AND SCL
L2	5 S L1 AND HEMATOPOI? STEM CELL?
L3	5 DUP REM L2 (0 DUPLICATES REMOVED)
L4	29844 S HEMATOPOI? STEM CELL?
L5	529 S L4 (5A) (ISOLAT? OR IDENTIF? OR SORT?)
L6	0 S L5 AND REPORTER AND GENOMIC LOC?
L7	4 S L5 AND REPORTER
L8	67 S L5 AND MARKER
L9	116 S L5 AND MARKER?
L10	4 DUP REM L7 (0 DUPLICATES REMOVED)

=> s l9 and Ikaros

L11 1 L9 AND IKAROS

=> d bib abs

L11 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS ON STN

AN 2002:637808 CAPLUS

DN 137:152031

TI Stem cell self-renewal and lineage commitment

IN Chan, Chang-zheng; Lodish, Harvey F.

PA Whithead Institute for Biomedical Research, USA

SO PCT Int. Appl., 36 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002064756	A2	20020822	WO 2002-US4459	20020215
WO 2002064756	C2	20021114		
WO 2002064756	A3	20030109		
WO 2002064756	C1	20030410		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002168660 A1 20021114 US 2002-77178 20020215

PRAI US 2001-269060P P 20010215

AB Methods of marking pluripotent cells, such as stem cells, particularly
 hematopoietic ***stem*** ***cells*** ; methods of
 detecting/ ***identifying*** , enriching, selecting and monitoring
 pluripotent cells (stem cells); DNA constructs useful in the methods; stem
 cells, such as ***hematopoietic*** ***stem*** ***cells*** ,
 identified by the method; as well as lineage-specific cells
 identified by the method; and uses for the cells are subjects of this
 invention. The cells are marked by targeting reporter genes into loci
 that are functionally specific and important for hematopoietic stem cell
 activity (e.g., self-renewal or lineage commitment). Combinations of
 targeted ***markers*** are used to provide phys. and functional
 identities for the cells. Two loci, stem cell leukemia (SCL) and
 ikaros , were targeted using HuCD4/RES/puro and .beta.neo(lacZneo)
 reporter cassettes, resp.

=> s l9 and SCL
 L12 1 L9 AND SCL

=> d bib abs

L12 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2002:637806 CAPLUS
 DN 137:152031
 TI Stem cell self-renewal and lineage commitment
 IN Chan, Chang-zheng; Lodish, Harvey F.
 PA Whithead Institute for Biomedical Research, USA
 SO PCT Int. Appl., 38 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002064756	A2	20020822	WO 2002-US4459	20020215
WO 2002064756	C2	20021114		
WO 2002064756	A3	20030109		
WO 2002064756	C1	20030410		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002168660 A1 20021114 US 2002-77178 20020215

PRAI US 2001-269060P P 20010215

AB Methods of marking pluripotent cells, such as stem cells, particularly
 hematopoietic ***stem*** ***cells*** ; methods of
 detecting/ ***identifying*** , enriching, selecting and monitoring
 pluripotent cells (stem cells); DNA constructs useful in the methods; stem
 cells, such as ***hematopoietic*** ***stem*** ***cells*** ,
 identified by the method; as well as lineage-specific cells
 identified by the method; and uses for the cells are subjects of this
 invention. The cells are marked by targeting reporter genes into loci
 that are functionally specific and important for hematopoietic stem cell
 activity (e.g., self-renewal or lineage commitment). Combinations of
 targeted ***markers*** are used to provide phys. and functional
 identities for the cells. Two loci, stem cell leukemia (***SCL***)
 and Ikaros, were targeted using HuCD4/RES/puro and .beta.neo(lacZneo)
 reporter cassettes, resp.

=> d his

(FILE 'HOME' ENTERED AT 16:01:52 ON 12 FEB 2004)

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 16:02:00 ON 12 FEB 2004

L1 12 S IKAROS AND SCL
 L2 5 S L1 AND HEMATOPOI? STEM CELL?
 L3 5 DUP REM L2 (0 DUPLICATES REMOVED)
 L4 29844 S HEMATOPOI? STEM CELL?
 L5 529 S L4 (5A) (ISOLAT? OR IDENTIF? OR SORT?)
 L6 0 S L5 AND REPORTER AND GENOMIC LOC?
 L7 4 S L5 AND REPORTER
 L8 67 S L5 AND MARKER
 L9 116 S L5 AND MARKER?
 L10 4 DUP REM L7 (0 DUPLICATES REMOVED)
 L11 1 S L9 AND IKAROS

L12 1 S L9 AND SCL

=> l5 and (ikaros or scl)
 L5 IS NOT A RECOGNIZED COMMAND
 The previous command name entered was not recognized by the system.
 For a list of commands available to you in the current file, enter
 "HELP COMMANDS" at an arrow prompt (=>).

=> s l5 and (ikaros or scl)
 L13 6 L5 AND (IKAROS OR SCL)

=> dup rem l13
 PROCESSING COMPLETED FOR L13
 L14 3 DUP REM L13 (3 DUPLICATES REMOVED)

=> d bib abs 1-
 YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):y

L14 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2002:637806 CAPLUS
 DN 137:152031
 TI Stem cell self-renewal and lineage commitment
 IN Chan, Chang-zheng; Lodish, Harvey F.
 PA Whithead Institute for Biomedical Research, USA
 SO PCT Int. Appl., 38 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002064756	A2	20020822	WO 2002-US4459	20020215
WO 2002064756	C2	20021114		
WO 2002064756	A3	20030109		
WO 2002064756	C1	20030410		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002168660 A1 20021114 US 2002-77178 20020215

PRAI US 2001-269060P P 20010215

AB Methods of marking pluripotent cells, such as stem cells, particularly
 hematopoietic ***stem*** ***cells*** ; methods of
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 pluripotent cells (stem cells); DNA constructs useful in the methods; stem
 cells, such as ***hematopoietic*** ***stem*** ***cells*** ,
 identified by the method; as well as lineage-specific cells
 identified by the method; and uses for the cells are subjects of this
 invention. The cells are marked by targeting reporter genes into loci
 that are functionally specific and important for hematopoietic stem cell
 activity (e.g., self-renewal or lineage commitment). Combinations of
 targeted markers are used to provide phys. and functional identities for
 the cells. Two loci, stem cell leukemia (***SCL***) and
 ikaros , were targeted using HuCD4/RES/puro and .beta.neo(lacZneo)
 reporter cassettes, resp.

L14 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS
 INC. on STN
 DUPLICATE 1
 AN 1999:111594 BIOSIS
 DN PREV199900111594
 TI Recent progress in ***identifying*** genes regulating
 hematopoietic ***stem*** ***cell*** function and fate.
 AU Jordan, Craig T. [Reprint author]; Van Zant, Gary
 CS Blood Marrow Transplantation Program, Markey-Cancer Center, 800 Rose
 Street Room CC405, University Kentucky Medical Center, Lexington, KY
 40536, USA
 SO Current Opinion in Cell Biology, (Dec., 1998) Vol. 10, No. 6, pp. 716-720.
 print.
 CODEN: COCBE3. ISSN: 0955-0674.
 DT Article
 General Review; (Literature Review)
 LA English
 ED Entered STN: 12 Mar 1999
 Last Updated on STN: 12 Mar 1999

L14 ANSWER 3 OF 3 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL
 RIGHTS RESERVED.
 on STN DUPLICATE 2
 AN 1998142812 EMBASE
 TI Transcriptional regulation of B-cell differentiation.
 AU Reya T.; Grosschedl R.
 CS R. Grosschedl, Howard Hughes Medical Institute, Department Microbiology
 Immunology, University of California, San Francisco, CA 94143-0414, United
 States. rgross@itsa.ucsf.edu
 SO Current Opinion in Immunology, (1998) 10/2 (158-165).
 Refs: 64

ISSN: 0952-7915 CODEN: COPIEL
CY United Kingdom
DT Journal; General Review
FS 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LA English
SL English
AB Transcription factors influence B cell differentiation by regulating the expression of numerous lineage-specific genes. Recent studies have identified factors that regulate differentiation of hematopoietic stem cells into B cell progenitors (PU.1 and Ikaros), and further differentiation of these progenitors into mature B cells (NF- κ B, E2A, early B cell factor [EBF] and B cell specific activator protein [BSAP]). In addition, these studies demonstrate that complex interactions and redundancies among transcription factors safeguard the precise patterns of gene expression required for normal B cell differentiation.

=> d his

(FILE 'HOME' ENTERED AT 16:01:52 ON 12 FEB 2004)

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 16:02:00 ON 12 FEB 2004

L1 12 S IKAROS AND SCL
L2 5 S L1 AND HEMATOPOI? STEM CELL?
L3 5 DUP REM L2 (0 DUPLICATES REMOVED)
L4 29844 S HEMATOPOI? STEM CELL?
L5 529 S L4 (5A) (ISOLAT? OR IDENTIF? OR SORT?)
L6 0 S L5 AND REPORTER AND GENOMIC LOC?
L7 4 S L5 AND REPORTER
L8 67 S L5 AND MARKER
L9 116 S L5 AND MARKER?
L10 4 DUP REM L7 (0 DUPLICATES REMOVED)
L11 1 S L9 AND IKAROS
L12 1 S L9 AND SCL
L13 6 S L5 AND (IKAROS OR SCL)
L14 3 DUP REM L13 (3 DUPLICATES REMOVED)

=> s l4 and (transduc? or transfec? or transfor?)

L15 4631 L4 AND (TRANSDUC? OR TRANSFEC? OR TRANSFOR?)

=> s l15 and reporter

L16 202 L15 AND REPORTER

=> s l16 and (identif? or isolat?)

L17 56 L16 AND (IDENTIF? OR ISOLAT?)

=> dup rem l17

PROCESSING COMPLETED FOR L17

L18 32 DUP REM L17 (24 DUPLICATES REMOVED)

=> s l18 and genomic loci

L19 0 L18 AND GENOMIC LOCI

=> d bib abs l18 1-

YOU HAVE REQUESTED DATA FROM 32 ANSWERS - CONTINUE? Y/(N):y

L18 ANSWER 1 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:652161 CAPLUS

DN 139:174825

TI Transgenic platelets carrying a reporter molecule and with a modified protein composition for identifying therapeutic target proteins

IN Peluso, Mario; Ungerer, Martin Pd; Gawaz, Meinrad; Massberg, Steffen; Laugwitz, Karl Ludwig; Gillitzer, Angelika

PA Procede G.m.b.H., Germany

SO Eur. Pat. Appl., 28 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI EP 1336846	A1	20030820	EP 2002-3352	20020213
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

WO 2003069339 A1 20030821 WO 2003-EP1450 20030213

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI EP 2002-3352 A 20020213

AB Transgenic platelets that can be used to study the role of specific proteins in interactions with the vascular endothelium and in clot formation in vivo carry a reporter mol., such as green fluorescent protein, and have altered levels of a platelet protein.

Further, methods of detg. platelet functions, notably aggregation and adhesion to endothelial cells are provided. Further, a novel method of prep. transgenic or modified platelets is provided. Methods of generating megakaryocytes from cultured hematopoietic stem cells, transforming them and producing platelets using adenoviral or retroviral vectors is described. Platelets produced by these megakaryocytes showed largely normal characteristics.
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 2 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 1

AN 2003:233906 BIOSIS

DN PREV200300233906

TI STAP-2/BKS, an adaptor/docking protein, modulates STAT3 activation in acute-phase response through its YXXQ motif.

AU Minoguchi, Mayu; Minoguchi, Shigeru; Aki, Daisuke; Joo, Akiko; Yamamoto, Tetsuya; Yumioka, Taro; Matsuda, Tadashi; Yoshimura, Akihiko [Reprint Author]

CS Division of Molecular and Cellular Immunology, Medical Institute of Bioregulation, Kyushu University, 3-1-1 Maidashi, Higashiku, Fukuoka, 812-8582, Japan
ykihiko@bioreg.kyushu-u.ac.jp

SO Journal of Biological Chemistry, (March 28 2003) Vol. 278, No. 13, pp. 11182-11189. print.

CODEN: JBCHA3. ISSN: 0021-9258.

DT Article

LA English

ED Entered STN: 14 May 2003

Last Updated on STN: 14 May 2003

AB As a c-fms-interacting protein, we cloned a novel adaptor molecule, signal-transducing adaptor protein-2 (STAP-2), which contains pleckstrin homology- and Src homology 2-like (PH and SRC) domains and a proline-rich region. STAP-2 is structurally related to STAP-1/BRDG1 (BCR downstream signaling-1), which we had cloned previously from hematopoietic stem cells. STAP-2 is a murine homologue of a recently identified adaptor molecule, BKS, a substrate of BRK tyrosine kinase. STAP-2 was tyrosine-phosphorylated and translocated to the plasma membrane in response to epidermal growth factor when overexpressed in fibroblastic cells. To define the function of STAP-2, we generated mice lacking the STAP-2 gene. STAP-2 mRNA was strongly induced in the liver in response to lipopolysaccharide and in isolated hepatocytes in response to interleukin-6. In the STAP-2-/- hepatocytes, the interleukin-6-induced expression of acute-phase (AP) genes and the tyrosine-phosphorylation level of STAT3 were reduced specifically at the late phase (6-24 h) of the response. These data indicate that STAP-2 plays a regulatory role in the AP response in systemic inflammation. STAP-2 contains a YXXQ motif in the C-terminal region that is a potential STAT3-binding site. Overexpression of wild-type STAP-2, but not of mutants lacking this motif, enhanced the AP response element reporter activity and an AP protein production. These data suggest that STAP-2 is a new class of adaptor molecule that modulates STAT3 activity through its YXXQ motif.

L18 ANSWER 3 OF 32 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN

AN 2003412057 EMBASE

TI Identification and characterization of mechanistically distinct inducers of gamma-globin transcription.

AU Haley J.D.; Smith D.E.; Schwedes J.; Brennan R.; Pearce C.; Moore C.; Wang F.; Petti F.; Grosfeld F.; Jane S.M.; Noguchi C.T.; Schechter A.N.

CS J.D. Haley, OSI Pharmaceuticals Inc., Farmingdale, NY 11735, United States. jhaley@osip.com

SO Biochemical Pharmacology, (1 Nov 2003) 66/9 (1755-1768).

Refs: 43

ISSN: 0006-2952 CODEN: BCPACA6

CY United States

DT Journal; Article

FS 030 Pharmacology

LA English

SL English

AB Inhibition of HbS polymerization is a major target for therapeutic approaches in sickle cell anemia. Toward this goal, initial efforts at pharmacological elevation of fetal hemoglobin (HbF) has shown therapeutic efficacy. In order to identify well-tolerated, novel agents that induce HbF in patients, we developed a high-throughput screening approach based on induction of gamma-globin gene expression in erythroid cells. We measured gamma-globin transcription in K562 cells transfected with either gamma promoter elements fused with the locus control region hypersensitivity site 2 and luciferase reporter gene (HS2-gamma.) or a beta.-yeast artificial chromosome in which the luciferase reporter gene was recombined into the gamma-globin coding sequences (gamma.YAC). Corresponding pharmacological increases in HbF protein were confirmed in both K562 cells and in human primary erythroid progenitor cells. Approximately 186,000 defined chemicals and fungal extracts were evaluated for their ability to increase gamma gene transcription in either HS2-gamma. or gamma.YAC models. Eleven distinct classes of compounds were identified, the majority of which were active within 24-48hr. The short chain hydroxamate-containing class generally exhibited delayed maximal activity, which continued to increase

transcription up to 120hr. The cyclic tetrapeptide OSI-2040 and the hydroxamates were shown to have histone deacetylase inhibitory activity. In primary hematopoietic progenitor cell cultures, OSI-2040 increased HbF by 4.5-fold at a concentration of only 40nM, comparable to the effects of hydroxyurea at 100.mu.M. This screening methodology successfully identifies active compounds for further mechanistic and preclinical evaluation as potential therapeutic agents for sickle cell anemia. .COPYRGT. 2003 Elsevier Inc. All rights reserved.

L18 ANSWER 4 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 2

AN 2003:137037 BIOSIS

DN PREV200300137037

TI Identification of the human HEX1/hExo1 gene promoter and characterization of elements responsible for promoter activity.

AU Ladd, Paula D.; Wilson, David M. II; Kelley, Mark R.; Skalniak, David G. [Reprint Author]

CS Department of Biochemistry and Molecular Biology, Indiana University School of Medicine, Indianapolis, IN, 46202, USA
dskalniak@iupui.edu

SO DNA Repair, (3 February 2003) Vol. 2, No. 2, pp. 187-198. print. ISSN: 1568-7864 (ISSN print).

DT Article

LA English

ED Entered STN: 12 Mar 2003

Last Updated on STN: 12 Mar 2003

AB HEX1/hExo1 is a Class III nuclease of the RAD2 family with 5' to 3' exonuclease and flap structure-specific endonuclease activities. HEX1/hExo1 is expressed at low levels in a wide variety of tissues, but at higher levels in fetal liver and adult bone marrow, suggesting HEX1/hExo1 is important for hematopoietic stem cell development. A putative HEX1/hExo1 promoter fragment extending from -6240 to +1600 bp exhibits cell-type specific activity in transient transfection assays. This fragment directs high luciferase reporter gene expression in the hematopoietic cell line K562, chronic myelogenous leukemia cells, but low luciferase expression in the non-hematopoietic cell line HeLa, human cervical carcinoma cells. Deletion studies identified a fragment spanning -688 to +1600 bp that exhibits full transcriptional activity while a slightly shorter fragment from -658 to +1600 bp exhibits significantly decreased promoter activity. In vitro binding assays revealed DNA-binding activities that interact with -687 to -681 bp and -665 to -658 bp elements. Oligonucleotide competition and antibody disruption studies determined that the transcription factor CREB-1 recognizes the -687 to -681 bp element, while transcription factors Sp1 and Sp3 recognize the -665 to -658 bp element. Mutation of either the CREB-1 or Sp1/Sp3 binding sites dramatically reduces HEX1/hExo1 promoter activity and elimination of both elements abolishes promoter activity.

L18 ANSWER 5 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 3

AN 2003:478511 BIOSIS

DN PREV200300478511

TI Labeling of hematopoietic stem and progenitor cells in novel activatable EGFP reporter mice.

AU Gilchrist, Derek S.; Ure, Jan; Hook, Lilian; Medvinsky, Alexander [Reprint Author]

CS Institute for Stem Cell Research, University of Edinburgh, West Main's Road, King's Buildings, Edinburgh, EH9 3JQ, UK
alexmed@sr0.bio.ed.ac.uk

SO Genesis The Journal of Genetics and Development, (July 2003) Vol. 36, No. 3, pp. 168-176. print. ISSN: 1528-954X (ISSN print).

DT Article

LA English

ED Entered STN: 15 Oct 2003

Last Updated on STN: 15 Oct 2003

AB Conditional activation and inactivation of genes using the Cre/loxP recombination system is a powerful tool for the analysis of gene function and for tracking cell fate. Here we report a novel silent EGFP reporter mouse line generated by enhancer trap technology using embryonic stem (ES) cells. Following transfection with the silent EGFP reporter construct, positive ES cell clones were treated with Cre recombinase. These "activated clones" were then further selected on the basis of ubiquitous EGFP expression during in vitro differentiation. The parental "silent" clones were then used for generating mice. Upon Cre-mediated activation in ovo tissues tested from these mice express EGFP. Long-term, strong and sustainable expression of EGFP is observed in most myeloid and lymphoid cells. As shown by in vivo transplantation assays, the majority of hematopoietic stem cells (HSCs) and spleen colony-forming units (CFU-S) reside within the EGFP positive fraction. Most in vitro colony-forming units (CFU-Cs) isolated from bone marrow also express EGFP. Thus, these reporter mice are useful for the analysis of Cre-mediated recombination in HSCs and hematopoietic progenitor cells. This, in combination with the high accessibility of the loxP sites, makes these mice a valuable tool for testing cell/tissue-specific Cre-expressing mice.

L18 ANSWER 6 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 4

AN 2003:46127 BIOSIS

DN PREV200300046127

TI Identification of endoglin as a functional marker that defines long-term repopulating hematopoietic stem cells.

AU Chen, Chang-Zheng; Li, Min; de Graaf, David; Monti, Stefano; Gottgens, Berthold; Sanchez, Maria-Jose; Lander, Eric S.; Golub, Todd R.; Green, Anthony R.; Lodish, Harvey F. [Reprint Author]

CS Whitehead Institute for Biomedical Research, Nine Cambridge Center, Cambridge, MA, 02142, USA
lodish@wi.mit.edu

SO Proceedings of the National Academy of Sciences of the United States of America, (November 28 2002) Vol. 99, No. 24, pp. 15468-15473. print. ISSN: 0027-8424 (ISSN print).

DT Article

LA English

ED Entered STN: 15 Jan 2003

Last Updated on STN: 15 Jan 2003

AB We describe a strategy to obtain highly enriched long-term repopulating (LTR) hematopoietic stem cells (HSCs) from bone marrow side-population (SP) cells by using a transgenic reporter gene driven by a stem cell enhancer. To analyze the gene-expression profile of the rare HSC population, we developed an amplification protocol termed "constant-ratio PCR," in which sample and control cDNAs are amplified in the same PCR. This protocol allowed us to identify genes differentially expressed in the enriched LTR-HSC population by oligonucleotide microarray analysis using as little as 1 ng of total RNA. Endoglin, an ancillary transforming growth factor beta receptor, was differentially expressed by the enriched HSCs. Importantly, endoglin-positive cells, which account for 20% of total SP cells, contain all the LTR-HSC activity within bone marrow SP. Our results demonstrate that endoglin, which plays important roles in angiogenesis and hematopoiesis, is a functional marker that defines LTR HSCs. Our overall strategy may be applicable for the identification of markers for other tissue-specific stem cells.

L18 ANSWER 7 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 5

AN 2002:588549 BIOSIS

DN PREV200200588549

TI Megakaryocytes derived from embryonic stem cells implicate CalDAG-GEFI in integrin signaling.

AU Eto, Koji; Murphy, Ronan; Kerrigan, Steve W.; Bertoni, Alessandra; Stuhlmann, Heidi; Nakano, Toru; Leavitt, Andrew D.; Shattil, Sanford J. [Reprint author]

CS Department of Cell Biology, Scripps Research Institute, La Jolla, CA, 92037, USA
shattil@scripps.edu

SO Proceedings of the National Academy of Sciences of the United States of America, (October 1, 2002) Vol. 99, No. 20, pp. 12819-12824. print. CODEN: PNASA6. ISSN: 0027-8424.

DT Article

LA English

ED Entered STN: 13 Nov 2002

Last Updated on STN: 13 Nov 2002

AB Fibrinogen binding to integrin alphaIIb beta3 mediates platelet aggregation and requires agonist-induced "inside-out" signals that increase alphaIIb beta3 affinity. Agonist regulation of alphaIIb beta3 also takes place in megakaryocytes, the bone marrow cells from which platelets are derived. To facilitate mechanistic studies of inside-out signaling, we describe here the generation of megakaryocytes in quantity from murine embryonic stem (ES) cells. Coculture of ES cells for 8-12 days with OP9 stromal cells in the presence of thrombopoietin, IL-6, and IL-11 resulted in the development of large, polyploid megakaryocytes that produced proplatelets. These cells expressed alphaIIb beta3 and platelet glycoprotein Ib/alpha but were devoid of hematopoietic stem cell, erythrocyte, and leukocyte markers. Mature megakaryocytes, but not megakaryocyte progenitors, specifically bound fibrinogen by way of alphaIIb beta3 in response to platelet agonists. Retrovirus-mediated expression of the reporter gene, green fluorescent protein, in ES cell-derived megakaryocytes did not affect viability or alphaIIb beta3 function. On the other hand, retroviral expression of CalDAG-GEFI, a Rap1 exchange factor identified by megakaryocyte gene profiling as a candidate integrin regulator, enhanced agonist-induced activation of Rap1b and fibrinogen binding to alphaIIb beta3 (P<0.01). These results establish that ES cells are a ready source of mature megakaryocytes for integrin studies and other biological applications, and they implicate CalDAG-GEFI in inside-out signaling to alphaIIb beta3.

L18 ANSWER 8 OF 32 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN

AN 2002096132 EMBASE

TI Deltex1 redirects lymphoid progenitors to the B cell lineage by antagonizing Notch1.

AU Izon D.J.; Aster J.C.; He Y.; Weng A.; Karnell F.G.; Patriub V.; Xu L.; Bakker S.; Rodriguez C.; Allman D.; Pear W.S.

CS W.S. Pear, Institute for Medicine/Engineering, Abramson Family Cancer Res. Inst., Univ. of Pennsylvania Medical Center, Philadelphia, PA 19104, United States. wpear@mail.med.upenn.edu

SO Immunity, (2002) 16/2 (231-243).

Refs: 57

ISSN: 1074-7613 CODEN: IUNIEH

CY United States

DT Journal; Article

FS 026 Immunology, Serology and Transplantation

029 Clinical Biochemistry

LA English

SL English

AB Notch1 signaling drives T cell development at the expense of B cell development from a common precursor, an effect that is dependent on a C-terminal Notch1 transcriptional activation domain. The function of Deltex1, initially ***identified*** as a positive modulator of Notch function in a genetic screen in *Drosophila*, is poorly understood. We now demonstrate that, in contrast to Notch1, enforced expression of Deltex1 in hematopoietic progenitors results in B cell development at the expense of T cell development in fetal thymic organ culture and in vivo. Consistent with these effects, Deltex1 antagonizes Notch1 signaling in transcriptional ***reporter*** assays by inhibiting coactivator recruitment. These data suggest that a balance of inductive Notch1 signals and inhibitory signals mediated through Deltex1 and other modulators regulate T-B lineage commitment.

L18 ANSWER 9 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 6

AN 2002:480481 BIOSIS

DN PREV200200480481

TI N-Acetyl-Ser-Asp-Lys-Pro inhibits phosphorylation of Smad2 in cardiac fibroblasts.

AU Pokharel, Saraswati; Rasoul, Saman; Roks, Anton J. M.; van Leeuwen, Rick E. W.; van Luyn, Marja J. A.; Deelman, Leo E.; Smits, Jos F.; Carretero, Oscar; van Gilst, Wiek H.; Pinto, Yigal M. [Reprint author]

CS Department of Cardiology, University Hospital Maastricht, Cardiovascular Research Institute Maastricht (CARIM), P Debyeilaan 25, 6202 GZ, Maastricht, Netherlands
ypi@cardio.azm.nl

SO Hypertension (Baltimore), (August, 2002) Vol. 40, No. 2, pp. 155-161. print.

CODEN: HPRTDN. ISSN: 0194-911X.

DT Article

LA English

ED Entered STN: 11 Sep 2002

Last Updated on STN: 11 Sep 2002

AB N-Acetyl-Ser-Asp-Lys-Pro (AcSDKP) is a specific substrate for the N-terminal site of ACE and increases 5-fold during ACE inhibitor therapy. It is known to inhibit the proliferation of ***hematopoietic*** ***stem*** ***cells*** and has also recently been reported to inhibit the growth of cardiac fibroblasts. We investigated its mode of action in cardiac fibroblasts by assessing its influence on ***transforming*** growth factor beta1 (TGFbeta1)-mediated Smad signaling. AcSDKP inhibited the proliferation of ***isolated*** cardiac fibroblasts ($P < 0.05$) but significantly stimulated the proliferation of vascular smooth muscle cells. Flow cytometry of rat cardiac fibroblasts treated with AcSDKP showed significant inhibition of the progression of cells from G0/G1 phase to S phase of the cell cycle. In cardiac fibroblasts ***transfected*** with a Smad-sensitive luciferase ***reporter*** construct, AcSDKP decreased luciferase activity by 55+-9.7% ($P = 0.01$). Moreover, phosphorylation and nuclear translocation of Smad2 was decreased in cardiac fibroblasts treated with AcSDKP. To conclude, AcSDKP inhibits the growth of cardiac fibroblasts and also inhibits TGFbeta1-stimulated phosphorylation of Smad2. Because AcSDKP increases substantially during ACE inhibitor therapy, this suggests a novel pathway independent of angiotensin II, by which ACE inhibitors can inhibit cardiac fibrosis.

L18 ANSWER 10 OF 32 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN

AN 2002243468 EMBASE

TI Xenotransplant cardiac chimera: Immune tolerance of adult stem cells.

AU Saito T.; Kuang J.-Q.; Bittira B.; Al-Khaldi A.; Chiu R.C.-J.

CS Dr. R.C.-J. Chiu, Division of Cardiac Surgery, Montreal General Hospital, MUHC, 1650 Cedar Ave, Montreal, Que. H3G 1A4, Canada. rchiu@po-box.mcgill.ca

SO Annals of Thoracic Surgery, (2002) 74/1 (19-24).

Refs: 20

ISSN: 0003-4975 CODEN: ATHSAK

PUI S 0003-4975(02)03591-9

CY United States

DT Journal; Article

FS 009 Surgery

018 Cardiovascular Diseases and Cardiovascular Surgery

026 Immunology, Serology and Transplantation

LA English

SL English

AB Background. Bone marrow stromal cells have been shown to engraft into xenogeneic fetal recipients. In view of the potential clinical utility as an alternative source for cellular and gene therapies, we studied the fate of xenogeneic marrow stromal cells after their systemic transplantation into fully immunocompetent adult recipients without immunosuppression. Methods. Bone marrow stromal cells were ***isolated*** from C57B1/6 mice and retrovirally ***transduced*** with LacZ ***reporter***

gene for cell labeling. We then injected 6×10^6 labeled cells into immunocompetent adult Lewis rats. One week later, the recipient animals underwent coronary artery ligation and were sacrificed at various time points ranging from 1 day to 12 weeks after ligation. Hearts, blood, and bone marrow samples were collected for histologic and immunohistochemical studies. Results. Labeled mice cells engrafted into the bone marrow cavities of the recipient rats for at least 13 weeks after transplantation without any immunosuppression. On the other hand, circulating mice cells were positive only for the animals with 1-day-old myocardial infarction. At various time points, numerous mice cells could be found in the infarcted myocardium that were not seen before coronary ligation. Some of these cells subsequently showed positive staining for cardiomyocyte specific proteins, while other labeled cells participated in angiogenesis in the infarcted area. Conclusions. The marrow stromal cells are adult stem cells with unique immunologic tolerance allowing their engraftment into a xenogeneic environment, while preserving their ability to be recruited to an injured myocardium by way of the bloodstream and to undergo differentiation to form a stable cardiac chimera. .COPYRG. 2002 by The Society of Thoracic Surgeons.

L18 ANSWER 11 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

AN 2003:356973 BIOSIS

DN PREV200300356973

TI Mapping Critical Cis-Elements Necessary for Human CD34 Gene Expression.

AU Okuno, Yutaka [Reprint Author]; Radomska, Hanna S.; Huettnet, Claudia S.; Iwasaki, Hiromi; Akashi, Koichi; Tenen, Daniel G.

CS Department of Internal Medicine II, Kumamoto University School of Medicine, Kumamoto, Kumamoto, Japan

SO Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 2839. print. Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.

CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)

Conference; (Meeting Poster)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 6 Aug 2003

Last Updated on STN: 6 Aug 2003

AB Previously, we reported that human CD34 flanking sequences extending from -18 kb to -10 kb 5' of the gene and/or from +42 kb to +50 kb 3' using critical cis-elements directing human CD34 expression in vivo using transgenic mice models employing various fragments derived from a large human genomic PAC clone including the entire hCD34 genomic sequence. All of these transgenic mice expressed human CD34 antigen in the majority of the ***hematopoietic*** ***stem*** ***cells*** (HSC) fraction, and functional assays confirmed that such cells conferred long-term reconstitution of lethally irradiated mice. Therefore we concluded that these critical cis-elements are necessary for human CD34 expression in HSC. To further localize the critical cis-elements for human CD34 expression, we used several different strategies. We first performed DNaseI hypersensitivity assays to localize open chromatin structures in the human CD34 gene in several human myeloblastic cell lines. We detected one DNaseI hypersensitive site -12.5 kb upstream of the transcription start site (TSS) of the human CD34 gene in the human myeloblastic CD34+ KG1a cell line. In contrast, there are several DNaseI hypersensitive sites in the region located between +42 kb to +50 kb 3' downstream of the human CD34 TSS, including sites at +43 kb, +44 kb, +48 kb, and +50 kb. In addition, we performed a homology search of the -18 kb to -10 kb human CD34 5' flanking sequence and +42 kb to +50 kb human CD34 3' flanking sequence, comparing it with the murine CD34 genomic sequence. While no homologous region could be ***identified*** in the 5' upstream sequence, there was one highly conserved region located +45 kb downstream of the transcription start site. To determine the importance of this region for human CD34 gene regulation, we amplified a 900 bp genomic DNA fragment including this 3' conserved region and subcloned it either 5' or 3' of a DNA fragment which included a human CD34 promoter and GFP ***reporter*** gene (hCD34-EGFP) to assess its function in stably ***transfected*** cell lines. This 3' conserved region directed high levels of GFP ***reporter*** expression, proving this region has at least one critical cis-element for hCD34 gene expression. In spite of the lack of homology in the 5' upstream region, we used a similar strategy to localize critical cis-elements within the -18 kb to -10 kb 5' upstream region. By successive deletion analysis of the DNA fragment that conferring high level GFP expression in the murine CD34+ 416B cell line, we localized the 5' distal control region to a 500 bp fragment located approximately 15 kb upstream of the TSS. We are currently in the process of generating transgenic mice with these 5' and 3' critical cis-elements to determine the importance of these regions for expression of the human CD34 gene in HSC in vivo.

L18 ANSWER 12 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

AN 2003:335762 BIOSIS

DN PREV200300335762

TI TGFbeta Induced Growth Arrest of Human Hematopoietic Cells Requires p57KIP2 Upregulation.

AU Scandura, Joseph M. [Reprint Author]; Bocconi, Piericola [Reprint Author]; Nimer, Stephen D. [Reprint Author]

CS Laboratory of Molecular Aspects of Hematopoiesis, Sloan-Kettering Institute, New York, NY, USA

SO Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 1162. print.

Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.

CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)

Conference; (Meeting Poster)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 23 Jul 2003

Last Updated on STN: 23 Jul 2003

AB TGFbeta is one of few known negative regulators of hematopoiesis, yet the mechanisms by which it affects growth arrest and stem cell quiescence are poorly understood. In epithelial cells, TGFbeta can trigger cell cycle arrest by upregulating growth inhibiting proteins such as the cyclin-dependent kinase (CDK) inhibitors (p15INK4b, p21CIP1/WAF1, and p27KIP1) while downmodulating growth stimulating proteins, notably, c-Myc. p21WAF/CIP1 plays an important role controlling the quiescence of normal ***hematopoietic*** ***stem*** ***cells*** (Cheng et al. 2000b), while p27KIP1, which is expressed in both ***hematopoietic*** ***stem*** ***cells*** and progenitor cells, plays a key role in determining the number of more mature hematopoietic progenitors (Cheng et al. 2000a). However, neither p21WAF/CIP1 nor p27KIP1 appear to be required for the inhibition of ***hematopoietic*** ***stem*** ***cell*** or progenitor cell growth by TGFbeta, as mice lacking these CDKIs retain full responsiveness to the growth inhibitory effects of TGFbeta (Cheng et al. 2001). Using purified, human CD34-positive primary hematopoietic progenitor/stem cells, and microarray analysis, we ***identified*** p57KIP2 as being the CDK inhibitor most rapidly and most robustly induced by TGFbeta. This upregulation occurs well in advance of TGFbeta induced G1 cell cycle arrest and persists for at least 30 hours after stimulation. The TGFbeta-induced upregulation of p57KIP2 mRNA is tightly correlated with expression of p57KIP2 protein and is transcriptional in nature. Using a series of ***reporter*** gene constructs driven by regions of the p57KIP2 promoter, we found two regions that are important in the TGFbeta-regulated expression of this CDKI. A highly GC-rich region, just upstream of the TATA box, is responsible for the TGFbeta-responsiveness of the ***reporter*** gene, whereas a second region, located between -595 and -165, contributes to the basal activity of the promoter and determines the absolute magnitude of expression when induced by TGFbeta. That p57KIP2 was the only CDKI ***identified*** as an immediate early target of TGFbeta in hematopoietic cells suggested that it could function as a primary effector of TGFbeta-mediated cytostasis. Consistent with this hypothesis we found that using siRNA to block the TGFbeta-mediated upregulation of p57KIP2 abrogated the growth inhibitory effects of TGFbeta in hematopoietic cells and demonstrated that the upregulation of p57KIP2 is required for the cytostatic effects of TGFbeta in this cell type. p57KIP2 is a putative tumor suppressor gene, which is located within a maternally-imprinted region of chromosome 11p15.5. We have documented the mono-allelic expression of p57KIP2 in normal human cord blood CD34+ hematopoietic progenitor cells demonstrating the gene is imprinted in hematopoietic cells. The imprinted loss of one allele may be important in several malignancies including AML where epigenetic silencing occurs in up to 30% of patients (Kikuchi et al. 2002). Further studies of TGFbeta and p57KIP2 regulation in leukemia are ongoing.

L18 ANSWER 13 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 7

AN 2001:471087 BIOSIS

DN PREV200100471087

TI HOXB4 overexpression mediates very rapid stem cell regeneration and competitive hematopoietic repopulation.

AU Antonchuk, Jennifer; Sauvageau, Guy; Humphries, R. Keith [Reprint author]

CS Terry Fox Laboratory, BC Cancer Agency, 601 West 10th Avenue, Vancouver, British Columbia, V5Z 1L3, Canada
khumphri@bccancer.bc.ca

SO Experimental Hematology (Charlottesville), (September, 2001) Vol. 29, No. 9, pp. 1125-1134. print.

CODEN: EXHMA6. ISSN: 0301-472X.

DT Article

LA English

ED Entered STN: 3 Oct 2001

Last Updated on STN: 23 Feb 2002

AB Objective. Hox transcription factors have emerged as important regulators of hematopoiesis. In particular, we have shown that overexpression of HOXB4 in mouse bone marrow can greatly enhance the level of ***hematopoietic*** ***stem*** ***cell*** (HSC) regeneration achieved at late times (> 4 months) posttransplantation. The objective of this study was to resolve if HOXB4 increases the rate and/or duration of HSC regeneration, and also to see if this enhancement was associated with impaired production of end cells or would lead to competitive reconstitution of all compartments. Methods. Retroviral vectors were generated with the GFP ***reporter*** gene +/- HOXB4 to enable the ***isolation*** and direct tracking of ***transduced*** cells in culture or following transplantation. Stem cell recovery was measured by limit dilution assay for long-term competitive repopulating cells (CRU). Results. HOXB4-overexpressing cells have enhanced growth in vitro, as demonstrated by their rapid dominance in mixed cultures and their shortened population doubling time. Furthermore, HOXB4- ***transduced*** cells have a marked competitive repopulating advantage in vivo in both primitive and mature compartments. CRU recovery in HOXB4 recipients was extremely rapid, reaching 25% of normal by 14 days posttransplant or some

80-fold greater than control transplant recipients, and attaining normal numbers by 12 weeks. Mice transplanted with even higher numbers of HOXB4- ***transduced*** CRU regenerated up to but not beyond the normal CRU levels. Conclusion. HOXB4 is a potent enhancer of primitive hematopoietic cell growth, likely by increasing self-renewal probability but without impairing homeostatic control of HSC population size or the rate of production and maintenance of mature end cells.

L18 ANSWER 14 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

AN 2002:261581 BIOSIS

DN PREV200200261581

TI The NF-Ya,b,c, complex activates the HOXB4 promoter and modulates hematopoiesis in vivo.

AU Zhu, Jiang [Reprint author]; Giannola, Diane [Reprint author]; Zhang, Yi [Reprint author]; Rivera, Adam J. [Reprint author]; Emerson, Stephen G. [Reprint author]

CS Department of Medicine and Pediatrics, University of Pennsylvania School of Medicine, Philadelphia, PA, USA

SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 829a-830a. print. Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.

CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 1 May 2002

Last Updated on STN: 1 May 2002

AB The homeobox gene products regulate the proliferation and differentiation of normal and malignant ***hematopoietic*** ***stem*** ***cells*** (HSCs). HOXB4 is preferentially expressed in primitive HSCs, and its overexpression potentiates HSC self-renewal in vivo. We previously ***identified*** two essential elements in the HOXB4 promoter, termed HxRE1 and HxRE2, and ***identified*** USF1/2 as the transcription factors that bind to HxRE2, but HxRE1-binding proteins were not found. We now show evidence that HxRE-1, a classic inverted Y box, is bound and activated by the regulatory heterotrimer NF-Y, which consists of three independently encoded subunits NF-Ya, NF-Yb and NF-Yc. Electrophoretic mobility supershift assays and chromatin immunoprecipitation assays from K562 cells showed that NF-Y specifically bound to HxRE-1 in vitro, and on intact chromatin in vivo. GST pull-down and co-immunoprecipitation assays showed that NF-Ya and NF-Yc subunits directly interacted with USF1/2. ***Transfection*** of equimolar ratios of expression plasmids encoding NF-Ya,b and c, along with USF-1 or USF-2, synergistically induce the expression of a HOXB4 promoter-luciferase ***reporter***. Thus, NF-Y is bound to HxRE-1, interacts with USF 1/2, and activates the HOXB4 promoter. Given the influence of HOXB4 in hematopoietic differentiation, and since NF-Ya is known to be regulated with cellular differentiation in many systems, we asked whether manipulation of NF-Ya expression could influence hematopoietic differentiation in normal cells. Full-length cDNAs encoding NF-Ya or NF-Yam, a dominant negative NF-Ya mutant were cloned into MigR-1/RES/EGFP retroviral vectors. These retroviruses, or control retroviruses not expressing NF-Y constructs, were produced in packaging lines, ***transduced*** into primitive murine HSCs (post-5FU or c-kit/sca1+Lin-), and then transplanted into lethally irradiated syngeneic mice. Four weeks following BMT, Gr-1+EGFP and Mac1+EGFP BM

and spleen cells were greatly reduced in mice transplanted with NF-Ya infected, and increased in mice transplanted with NF-Yam infected HSCs. Bone marrow from NF-Yam mice also had lower numbers of Sca-1+Lin-stem cell pool. In vitro methylcellulose assays from NF-Ya and NF-Yam- ***transduced*** BM showed similar effects on myeloid differentiation. Thus, NF-Ya overexpression in vivo blocks hematopoietic differentiation, and prevention of normal NF-Ya expression shifts hematopoiesis out of the stem cell pool. Taken together, these results indicate that the NF-Y complex is a critical activator of the HOXB4 promoter, and suggest that the regulated activity of NF-Y may play a physiologic role in the maintenance and self-renewal of HSCs.

L18 ANSWER 15 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

AN 2002:241168 BIOSIS

DN PREV200200241168

TI Functional platelet production from embryonic stem (ES) cells in vitro.

AU Kohata, Satoshi [Reprint author]; Imagawa, Yasunori [Reprint author]; Fujimoto, Tetsuro-Takahiro [Reprint author]; Fujimura, Kingo [Reprint author]

CS Department of Clinical Pharmaceutical Science, Graduate School of Medicine, Hiroshima University, Hiroshima, Japan

SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 454a. print. Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.

CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 17 Apr 2002

Last Updated on STN: 17 Apr 2002

AB Various culture systems demonstrating megakaryocyte maturation and proplatelet formation from hematopoietic progenitor cells have been

described. A potentially limiting factor in such strategies to generate sufficient amount of megakaryocytes for research or clinical application is the number of obtained CD34 stem cells and the difficulties of in vitro expansion of these cells. Embryonic stem (ES) cells are good another source since these cells possess the property of rapid proliferation and the capacity to differentiate to a variety of cell types. Several techniques have been established to promote in vitro differentiation of ES cells to hematopoietic cell lineages including megakaryocytes. In this study, we utilized the coculture system with the stromal cell line OP9 to generate mature megakaryocytes from ES cells and ***identified*** the functional platelets produced in the culture supernatants. ES cell line, TT2, which was established from an F1 embryo between a C57B/6 female and a CBA male mouse, was cultured on the OP9 layers which induced the differentiation to hematopoietic progenitors without formation of embryonic bodies. On day 5, cells were passed onto fresh OP9 cells in the presence of TPO. After 10-14 days, most of the cells showed morphological feature of megakaryocytes and numerous proplatelets were observed. The differentiation was confirmed by immunostaining with anti-GPIIb-IIIa antibody and AchE staining. In addition, platelet-sized particles collected from culture supernatants were also GPIIb-IIIa-positive by flow cytometric analysis. Functionally, these particles aggregated in response to thrombin plus fibrinogen. We concluded that functional platelets were released from mature megakaryocytes derived from ES cells. 104 ES cells finally produced as many as 108 platelets. We next prepared the constructs in which actin promoter or megakaryocyte-specific PF4 promoter was linked to the green fluorescence protein (GFP) as a ***reporter*** gene. ES cells were ***transfected*** with these constructs by electroporation, and the positive clones were selected with G418. When differentiation was started with these cells, GFP-positive megakaryocytes displaying proplatelets were observed in both cases. Furthermore, platelets in the supernatants were also both GFP and GPIIb-IIIa-positive. These data suggest potential utility of the ES cell-derived platelets as a substitute for platelet transfusion. Combined with the ability of genetic manipulation of ES cells, this system will facilitate the functional studies using the gene-transferred platelets, and might be a future approach for the treatment of platelet dysfunction.

L18 ANSWER 16 OF 32 CAPLUS COPYRIGHT 2004 ACS ON STN

AN 2001:37749 CAPLUS

DN 135:117681

TI Simplified retroviral vector GCsap with murine stem cell virus long terminal repeat allows high and continued expression of enhanced green fluorescent protein by human hematopoietic progenitors engrafted in nonobese diabetic/severe combined immunodeficient mice

AU Kaneko, Shin; Onodera, Masafumi; Fujiki, Yutaka; Nagasawa, Toshiro; Nakauchi, Hiromitsu

CS Department of Immunology, Institute of Basic Medical Sciences, University of Tsukuba, Tsukuba, 305-8575, Japan

SO Human Gene Therapy (2001), 12(1), 35-44

CODEN: HGTHE3; ISSN: 1043-0342

PB Mary Ann Liebert, Inc.

DT Journal

LA English

AB Despite efforts toward improvements in retrovirus-mediated gene transfer, stable high-level expression of a therapeutic gene in human ***hematopoietic*** ***stem*** ***cells*** remains a great challenge. We have evaluated the efficiency of different viral long terminal repeats (LTRs) in long-term expression of a transgene in vivo, using severe combined immunodeficiency (SCID)-repopulating cell assays. Vectors used were variants of the simplified retroviral vector GCsap with the different LTRs of Moloney murine leukemia virus (MLV), myeloproliferative sarcoma virus (MPSV), and murine stem cell virus (MSCV). The enhanced green fluorescent protein (EGFP) gene was used as a marker to assess levels of ***transduction*** efficiency. CD34+ cells ***isolated*** from human cord blood were ***transduced*** by exposure to virus-contg. supernatants on fibronectin fragments and in the presence of stem cell factor, interleukin 6, Flt-3 ligand, and thrombopoietin, and then transplanted into nonobese diabetic/SCID mice. Engraftment of human cells highly expressing EGFP, with differentiation along multiple cell lineages, was demonstrated for up to 18 wk posttransplant, although the three different vectors showed different ***transduction*** frequencies (MLV, <0.1-33.2%; MPSV, <0.1-22.8%; MSCV, 0.3-51.7%). Of importance is that high-level ***transduction*** frequencies in human progenitor cells were also confirmed by colony-forming cell assays using bone marrow from transplanted mice, in which EGFP-expressing, highly proliferative potential colonies were obsd. by fluorescence microscopy. In these mice the vector carrying the MSCV LTR generated more EGFP-expressing human cells than did either of the other two constructs, indicating that GCsap carrying the MSCV LTR may be an efficient tool for stem cell gene therapy.

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 17 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS

INC. ON STN

AN 2001:314046 BIOSIS

DN PREV200100314046

TI Targeted integration of a GFP ***reporter*** into the SCA-1 locus results in high level expression in hematopoietic cells of transgenic mice.

AU Meek, Sally C. [Reprint author]; Graubert, Timothy A. [Reprint author]

CS Internal Medicine, Division of Oncology, Section of Stem Cell Biology,

Washington University School of Medicine, St. Louis, MO, USA

SO Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 663a, print. Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.

CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 4 Jul 2001

Last Updated on STN: 19 Feb 2002

AB To develop a system for targeting expression of genes to the ***hematopoietic*** ***stem*** ***cell*** compartment, we employed Sca-1 (Ly-6A/E), a well-characterized marker of murine ***hematopoietic*** ***stem*** ***cells***. We assembled a targeting vector consisting of 5.2 kb of Sca-1 genomic sequence isogenic to our embryonic stem (ES) cell line (129/SvJ strain, Ly-6A.2 allele). An enhanced green fluorescent protein (GFP) cDNA (Clontech Labs, Palo Alto, CA) was inserted immediately following the Sca-1 Kozak sequence in exon II. We removed the Sca-1 initiation codon and left the remaining genomic sequences intact. A LoxP-flanked PGK-Neo cassette was subcloned downstream of the GFP ***reporter***. As an initial test of this construct, we electroporated it into EL-4 cells, a murine B cell line that constitutively expresses high levels of Sca-1. A small fraction (0.5-1.5%) of transiently ***transfected*** cells demonstrated detectable GFP expression. A wide range of GFP activity was evident in stable clones, suggesting that our targeting construct is capable of directing high level expression after random integration into hematopoietic cells. We then electroporated this construct into RW4 ES cells and ***identified*** three clones that had undergone homologous recombination. One of these clones was transiently ***transfected*** with a plasmid encoding the Cre recombinase. We derived twelve correctly targeted clones which had undergone excision of the PGK-Neo cassette. At this time, data is available from analysis of five chimeric founders obtained by injection of C57BL/6 blastocysts with one of the PGK-Neo (+) clones. Flow cytometric analysis of peripheral blood using the Ly-9.1 congenic marker demonstrated ES cell-derived hematopoiesis in a large proportion of leukocytes (range 31.8-73.6%) in these chimeric mice. GFP+ cells are easily detectable in peripheral blood from each of the animals, indicating that the Sca-1 targeting strategy successfully marked hematopoietic cells. The frequency of GFP+ cells correlates well with the degree of 129/SvJ chimerism and is surprisingly high (range 58.8-68.2% of ES-derived hematopoietic cells). However, approximately half of the GFP+ cells in each animal are Sca-1 negative, suggesting either increased post-transcriptional stability of the GFP ***reporter*** relative to the endogenous Sca-1 allele, or that expression of the targeted allele is dysregulated (possibly due to the retained PGK-Neo cassette). Analysis of F1 heterozygous mice (+/-PGK-Neo) should allow us to evaluate whether this system provides a valid strategy for genetically targeting ***hematopoietic*** ***stem*** ***cells*** in vivo.

L18 ANSWER 18 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. ON STN

AN 2001:313999 BIOSIS

DN PREV200100313999

TI High level of transgene expression in NOD/SCID-repopulating cells using third generation of lentiviral vectors.

AU Scherr, Michaela [Reprint author]; Battmer, Karin [Reprint author]; Eder, Matthias [Reprint author]; Ganser, Arnold [Reprint author]; Grez, Manuel

CS Hematology and Oncology, Hannover Medical School, Hannover, Germany

SO Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 430a, print.

Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.

CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

Conference; (Meeting Poster)

LA English

ED Entered STN: 4 Jul 2001

Last Updated on STN: 19 Feb 2002

AB Lentiviral vectors derived from human immunodeficiency virus-1 (HIV-1) represent a novel therapeutic tool for the ***transduction*** of non-dividing cells. Since hematopoietic stem and progenitor cells are usually in a non-cycling state, ***transduction*** using conventional retroviral vectors such as MLV requires cytokine stimulation that may reduce their repopulating ability. We therefore utilized HIV-1 based, VSV-G pseudotyped vector systems to avoid ex vivo stimulation of hematopoietic target cells. Replication-defective lentiviral vector particles encoding the green fluorescent protein as a ***reporter*** gene under the control of the human cytomegalovirus (CMV) major immediate early promoter were produced using the three-plasmid expression system in 293T human kidney cells. The vector particles were concentrated by anion exchange chromatography. This method allows the concentration of virus suspension up to 11 in a continuous flow system. We determined the number of lentivirus particles present in vector preparations by both real-time Taqman PCR as well as by monitoring GFP expression in 293T cells. Progenitor cells ***isolated*** from G-CSF mobilized peripheral blood mononuclear cells (PBMCs) were ***transduced*** twice with vectors concentrated by anion exchange chromatography (biological titer: 5X 10⁸ - 1X 10⁹ c.f.u./ml) under serum-free conditions in the absence of cytokines. ***Transfection*** efficiencies of the lentivirus at different MOI (MOI 3 and 27) was determined by flow cytometry. CD34+ cells were efficiently

transduced (12 - 45% respectively) following infection for less than 32 h as determined by conventional colony assay. To determine ***transduction*** of SCID-repopulating cells, CD34+ cells were injected via the tail vein into sublethally irradiated NOD/SCID mice. After seven weeks animals were analyzed for the presence of human leukocytes in bone marrow. We obtained high levels of NOD/SCID repopulating activity (40 to 80% human CD45+ cells) and an efficient transgene expression in myeloid and lymphoid lineages (up to 40-58%) by using a viral MOI of 27. These experiments demonstrate the potential of lentiviral-based gene transfer systems as an excellent tool for gene therapy applications.

L18 ANSWER 19 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 8

AN 2000:464037 BIOSIS

DN PREV20000464037

TI Lentiviral vector ***transduction*** of ***hematopoietic***

stem ***cells*** that mediate long-term reconstitution of lethally irradiated mice.

AU Chen, WenYong; Wu, Xiaoyun; Levasseur, Dana N.; Liu, Hongmei; Lai, Lili; Kappes, John C.; Townes, Tim M. [Reprint author]

CS Department of Biochemistry and Molecular Genetics, University of Alabama at Birmingham, 845 19th Street South, BBRB 870, Birmingham, AL, 35294, USA
SO Stem Cells (Miamisburg), (2000) Vol. 18, No. 5, pp. 352-359. print.
ISSN: 1066-5099.

DT Article

LA English

ED Entered STN: 25 Oct 2000

Last Updated on STN: 10 Jan 2002

AB Lentiviral vectors efficiently ***transduce*** human CD34+ cells that mediate long-term engraftment of nonobese diabetic/severe combined immunodeficient mice. However, hematopoiesis in these animals is abnormal. Typically, 95% of the human cells in peripheral blood are B lymphocytes. To determine whether lentiviral vectors efficiently ***transduce*** stem cells that maintain normal hematopoiesis in vivo, we ***isolated*** Sca-1+c-Kit+Lin- bone marrow cells from mice without 5-fluorouracil treatment, and ***transduced*** these cells in the absence of cytokine stimulation with a novel lentiviral vector containing a GFP (green fluorescent protein) ***reporter*** gene. These cells were transplanted into lethally irradiated C57BL/6 mice. In fully reconstituted animals, GFP expression was observed in 8.0% of peripheral blood mononuclear cells for 20 weeks posttransplantation. Lineage analysis demonstrated that a similar percentage (approximately 8.0%) of GFP-positive cells was detected in peripheral blood B cells, T cells, granulocytes and monocytes, bone marrow erythroid precursor cells, splenic B cells, and thymic T cells. In secondary transplant recipients, up to 20% of some lineages expressed GFP. Our results suggest that quiescent, ***hematopoietic*** ***stem*** ***cells*** are efficiently ***transduced*** by lentiviral vectors without impairing self-renewal and normal lineage specification in vivo. Efficient gene delivery into murine stem cells with lentiviral vectors will allow direct tests of genetic therapies in mouse models of hematopoietic diseases such as sickle cell anemia and thalassemia, in which corrected cells may have a selective survival advantage.

L18 ANSWER 20 OF 32 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN

AN 1998236070 EMBASE

TI ***Identification*** of a human immunodeficiency virus type 2 (HIV-2) encapsidation determinant and ***transduction*** of nondividing human cells by HIV-2-based lentivirus vectors.

AU Poeschla E.; Gilbert J.; Li X.; Huang S.; Ho A.; Wong-Staal F.
CS F. Wong-Staal, Department of Medicine 0665, University of California, 9500 Gilman Dr., San Diego, CA 92093-0665, United States. fwongstaal@ucsd.edu
SO Journal of Virology, (1998) 72/8 (6527-6536).

Refs: 66

ISSN: 0022-538X CODEN: JOVIAM

CY United States

DT Journal; Article

FS 004 Microbiology

LA English

SL English

AB Although previous lentivirus vector systems have used human immunodeficiency virus type 1 (HIV-1), HIV-2 is less pathogenic in humans and is amenable to pathogenicity testing in a primate model. In this study, an HIV-2 molecular clone that is infectious but apathogenic in macaques was used to first define cis-acting regions that can be deleted to prevent HIV-2 genomic encapsidation and replication without inhibiting vital gene expression. Lentivirus encapsidation determinants are complex and incompletely defined; for HIV-2, some deletions between the major 5' splice donor and the gag open reading frame have been shown to minimally affect encapsidation and replication. We find that a larger deletion (61 to 75 nucleotides) abrogates encapsidation and replication but does not diminish mRNA expression. This deletion was incorporated into a replication-defective, envelope-pseudotyped, three-plasmid HIV-2 lentivirus vector system that supplies HIV-2 Gag/Pol and accessory proteins in trans from an HIV-2 packaging plasmid. The HIV-2 vectors efficiently ***transduced*** marker genes into human T and monocytoid cell lines and, in contrast to a murine leukemia virus-based vector, into growth, arrested HeLa cells and terminally differentiated human macrophages and NTN2 neurons. Vector DNA could be detected in HIV-2 vector-***transduced*** nondividing CD34+ CD38- human hematopoietic progenitor

cells but not in those cells ***transduced*** with murine vectors. However, stable integration and expression of the ***reporter*** gene could not be detected in these hematopoietic progenitors, leaving open the question of the accessibility of these cells to stable lentivirus ***transduction***.

L18 ANSWER 21 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1998:665361 CAPLUS

DN 130:22468

TI Use of the green fluorescent protein as a marker to ***identify*** and track genetically modified hematopoietic cells

AU Persons, Derek A.; Allay, James A.; Riberd, Janice M.; Wersto, Robert P.; Donahue, Robert E.; Sorrentino, Brian P.; Nienhus, Arthur W.

CS Division of Experimental Hematology, Department of Hematology/Oncology, St. Jude Children's Research Hospital, Memphis, TN, 38105, USA

SO Nature Medicine (New York) (1998), 4(10), 1201-1205

CODEN: NAMEFI; ISSN: 1078-8956

PB Nature America

DT Journal

LA English

AB The utility of the green fluorescent protein (GFP) to serve as a marker to assess retroviral gene transfer into hematopoietic cells was described. Purification of genetically modified cells and the tracking of such cells following transplantation is a possible application for the method. The expression of GFP marker offers simplicity and high sensitivity that enables the facile analysis of clinical gene-marking protocols designed to optimize gene transfer into ***hematopoietic*** ***stem*** ***cells***.

RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L18 ANSWER 22 OF 32 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN

AN 1998185849 EMBASE

TI Gene transfer into human umbilical cord blood-derived CD34+ cells by particle-mediated gene transfer.

AU Verma S.; Woffendin C.; Bahner I.; Ranga U.; Xu L.; Yang Z.-Y.; King S.R.; Kohn D.B.; Nabel G.J.

CS G.J. Nabel, Howard Hughes Medical Institute, University Michigan Medical Center, Department of Internal Medicine, 1150 W Medical Center Drive, Ann Arbor, MI 48109-0650, United States

SO Gene Therapy, (1998) 5/5 (692-699).

Refs: 36

ISSN: 0969-7128 CODEN: GETHEC

CY United Kingdom

DT Journal; Article

FS 022 Human Genetics

025 Hematology

LA English

SL English

AB Delivery of genes into hematopoietic progenitor cells offers an attractive means for the introduction of corrective or protective genes into cells of both the myeloid and lymphoid lineage. Previously, investigators have often used murine retroviral vectors for gene delivery which require cells to be cycling for efficient delivery. We describe a nonviral method of gene delivery using particle-mediated gene transfer to obviate many disadvantages of viral vectors related to safety, production costs and the need for cell cycle proliferation. Using a CMV-CAT ***reporter*** plasmid, we show ***transfection*** of highly purified CD34+ cells ***isolated*** from umbilical cord blood. Effective gene transfer was shown in unstimulated and in growth-stimulated cells. Following ***transfection*** with a neomycin resistance gene, differentiation into cells of the myeloid lineage was observed, assayed by CFU-GM in the presence of G-418. Both unstimulated and stimulated cells gave rise to CFU-GM in the presence of G-418, indicating that stable expression of the neomycin resistance gene was maintained in early progenitors. These results demonstrate that particle-mediated gene transfer into human hematopoietic cells from umbilical cord blood can be achieved without affecting their CFU-GM differentiation potential. This gene transfer method offers an alternative approach to gene therapy studies involving human hematopoietic progenitor cells.

L18 ANSWER 23 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 9

AN 1998:135009 BIOSIS

DN PREV199800135009

TI Hematopoietic transcription factor GATA-2 activates transcription from HIV-1 long terminal repeat.

AU Towatari, Masayuki [Reprint author]; Kanei, Yukiko; Saito, Hidehiko; Hamaguchi, Michinari

CS First Dep. Internal Med., Nagoya University Sch. Med., Tsurumai-cho 65, Showa-ku, Nagoya 466, Japan

SO AIDS (London), (Feb. 12, 1998) Vol. 12, No. 3, pp. 253-259. print.

CODEN: AIDSET; ISSN: 0269-9370.

DT Article

LA English

ED Entered STN: 20 Mar 1998

Last Updated on STN: 20 Mar 1998

AB Objectives: To study the role of the hematopoietic transcription factor GATA-2 in long terminal repeat (LTR)-directed transcriptional activation

of HIV-1 in hematopoietic progenitor cells, and to investigate possible GATA-2 binding sites in HIV-1 LTR. Design and methods: Wild-type HIV-1 LTR, or mutants, ligated to a luciferase ***reporter*** gene with or without a GATA-2 expression vector, were ***transfected*** into COS cells, and standardized luciferase activity was examined. The binding activity of GATA-2 to these sites was examined by electrophoretic mobility shift assay. These wild-type or mutant ***reporter*** genes were also ***transfected*** into the murine hematopoietic progenitor cells, BAF3, in which GATA-2 was the predominantly expressed transcription factor of the GATA family, to assay LTR-directed transcription in intact hematopoietic machinery. Using a Tat expression plasmid for cotransfection, the influence of Tat protein on GATA-2-induced transactivation was determined. Results: In COS cells, LTR-dependent transactivation was highly enhanced by the coexpression of GATA-2. Experiments with mutant LTR suggested the presence of multiple GATA-2 binding sites, of which the major sites were ***identified***. Cotransfection of Tat with GATA-2 indicated that GATA-2 and Tat synergistically enhanced the transcriptional activity. ***Transfection*** experiments in BAF3 cells showed that the disruption of these GATA sites diminished LTR-driven activity to 40% of the wild-type. Conclusions: GATA-2 may be a key host cell regulator of HIV-1 expression in ***hematopoietic*** ***stem*** ***cells***. Manipulating this transactivation may represent a valuable approach to controlling virus production in infected hematopoietic progenitors. To elucidate the possible interaction between GATA-2 and Tat protein in vivo might give new insights to the mechanism of impaired hematopoiesis in AIDS patients.

L18 ANSWER 24 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 10

AN 1998:346574 BIOSIS

DN PREV199800346574

TI Sustained gene expression in retrovirally ***transduced***, engrafting human ***hematopoietic*** ***stem*** ***cells*** and their lympho-myeloid progeny.

AU Cheng, Linzhao; Du, Changchun; Lavau, Catherine; Chen, Shirley; Tong, Jie; Chen, Benjamin P.; Scollay, Roland; Hawley, Robert G.; Hill, Beth [Reprint author]

CS Systemix Inc., 3155 Porter Dr., Palo Alto, CA 94304, USA

SO Blood, (July 1, 1998) Vol. 92, No. 1, pp. 83-92. print.

CODEN: BLOOAW. ISSN: 0006-4971.

DT Article

LA English

ED Entered STN: 13 Aug 1998

Last Updated on STN: 13 Aug 1998

AB Inefficient retroviral-mediated gene transfer to human ***hematopoietic*** ***stem*** ***cells*** (HSC) and insufficient gene expression in progeny cells derived from ***transduced*** HSC are two major problems associated with HSC-based gene therapy. In this study we evaluated the ability of a murine stem cell virus (MSCV)-based retroviral vector carrying the low-affinity human nerve growth factor receptor (NGFR) gene as ***reporter*** to maintain gene expression in ***transduced*** human hematopoietic cells. CD34+ cells lacking lineage differentiation markers (CD34+Lin-) ***isolated*** from human bone marrow and mobilized peripheral blood were ***transduced*** using an optimized clinically applicable protocol. Under the conditions used, greater than 75% of the CD34+ cell population retained the Lin- phenotype after 4 days in culture and at least 30% of these expressed a high level of NGFR (NGFR+) as assessed by fluorescence-activated cell sorter analysis. When these CD34+Lin-NGFR+ cells sorted 2 days posttransduction were assayed in vitro in clonogenic and long-term stromal cultures, sustained ***reporter*** expression was observed in differentiated erythroid and myeloid cells derived from ***transduced*** progenitors, and in differentiated B-lineage cells after 6 weeks. Moreover, when these ***transduced*** CD34+Lin-NGFR+ cells were used to repopulate human bone grafts implanted in severe combined immunodeficient mice, MSCV-directed NGFR expression could be detected on 37% +/- 6% (n = 5) of the donor-type human cells recovered 9 weeks postinjection. These findings suggest potential utility of the MSCV retroviral vector in the development of effective therapies involving gene-modified HSC.

L18 ANSWER 25 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1998:622366 CAPLUS

DN 130:33626

TI Gene transfer into hematopoietic cells of mouse and its in vivo expression after transplantation

AU Zou, Ping; Lu, Huazhong; Xiang, Jianping

CS Institute Hematology, Tongji Medical University, Wuhan, 430022, Peop. Rep. China

SO Journal of Tongji Medical University (1998), 18(1), 46-48

CODEN: JTMUEI; ISSN: 0257-716X

PB Tongji Medical University

DT Journal

LA English

AB We have shown previously that high-efficient gene transfer can be attained in primary hematopoietic cells using liposome-mediated gene transfer strategy. In order to examine the stability of gene expression mediated by this gene ***transduction*** protocol, we obsd. the expression of marker gene in vivo by using bone marrow transplantation (BMT) to engraft lethally irradiated mouse with the genetically modified hematopoietic cells. The results showed that the mouse transplanted with appropriated

no. of ***transduced*** cells remained alive and healthy. The PCR anal. and G418 selection of the spleen colonies and bone marrow cells ***isolated*** from lethally irradiated animals 15 days and 30 days after injection of genetically modified bone marrow cells showed that the progeny cells of the ***transduced*** ***hematopoietic*** ***stem*** ***cells*** still contained and expressed the ***transduced*** genes, suggesting that the hematopoietic system is at least partially re-constructed by the stem cells with marker gene and that the stable expression of foreign genes in vivo can be attained by using this easy and harmless ***transduction*** protocol. These findings provide exptl. basis for clinician to further investigate the biol. of marrow reconstruction and the mechanism of leukemia relapse after BMT.

L18 ANSWER 26 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

AN 1998:71885 BIOSIS

DN PREV199800071885

TI Retroviral gene transfer into cord blood stem/progenitor cells using purified vector stocks.

AU Asch, Julie; Weinberg, Rona S.; Mueller, Lisa; Galperin, Yelena; Kiang, Lily; Jolly, Douglas; Isola, Luis M. [Reprint author]

CS Mount Sinai Sch. Med., One Gustave L. Levy Place, Box 1079, New York, NY 10029, USA

SO American Journal of Hematology, (Jan., 1998) Vol. 57, No. 1, pp. 16-23. print.

CODEN: AJHEDD. ISSN: 0361-8609.

DT Article

LA English

ED Entered STN: 24 Feb 1998

Last Updated on STN: 24 Feb 1998

AB Cord blood (CB) progenitor/stem cells (P/SC) are ideal targets for early gene therapy in individuals prenatally diagnosed with genetic disorders. Most retroviral ***transduction*** protocols were developed using adult peripheral blood stem cells (PBSC) and bone marrow (BM). Less is known about retroviral ***transduction*** of CB P/SC. We examined how timing, multiplicity of infection (MOI), and polycations in the ***transduction*** media affect ***transduction*** efficiency. Rates of ***transduction*** were determined in recently ***isolated*** CD34+ enriched CB cells and in colonies derived after various times in liquid cultures (LC). CB mononuclear cells (MNC) were separated by ficoll-hypaque centrifugation and enriched for CD34+ cells. Purity was assessed by flow cytometry. ***Transduction*** were performed with clinical-grade retroviral stocks at MOIs of 1-20. ***Transduction*** was performed with fetal bovine serum (FBS) or autologous plasma, IL-3, GM-CSF, IL-6, and SCF. The retroviral vector contained LacZ and neomycin resistance (neo) ***reporter*** genes. ***Transduction*** was determined by X-gal stain and by PCR amplification of the ***reporter*** genes. No drug selection was used. Twenty-five experiments were done. CB volumes ranged from 35-150 ml. MNC and CD34+ cell counts ranges were: 0.14-840 X 10⁶ and 0.1-4.2 X 10⁶, respectively. ***Transduction*** efficiency in liquid cultures ranged from 4-63%. Higher rates were seen using MOI gtoreq 10, 2 mug/ml polybrene, and 10% autologous CB plasma. In colonies, ***transduction*** rates were 63 to 72% by PCR and 32% by X-gal staining. In LTC-IC derived colonies, ***transduction*** was 7% by PCR. Short incubations of CD34+ CB cells with purified retroviral stocks, polybrene, and autologous sera result in high ***transduction*** rates of committed progenitors and moderately low efficiencies of ***transduction*** of LTC-IC in the absence of drug selection.

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on STN

AN 97286526 EMBASE

DN 1997286526

TI Regulation of CD34 expression in differentiating M1 cells.

AU Krause D.S.; Kapadia S.U.; Raj N.B.K.; May W.S.

CS Dr. W.S. May, Sealy Ctr. for Oncology/Hematology, University of Texas Medical Branch, 8.104 Medical Research Building, 301 University Boulevard, Galveston, TX 77555-0630, United States

SO Experimental Hematology, (1997) 25/10 (1051-1061).

Refs: 36

ISSN: 0301-472X CODEN: EXHEBH

CY United States

DT Journal; Article

FS 025 Hematology

026 Immunology, Serology and Transplantation

LA English

SL English

AB CD34 is a cell surface glycoprotein expressed on hematopoietic stem and progenitor cells, but not on mature blood cells. In the present study we found that CD34 downregulation during hematopoiesis occurred at the level of transcriptional initiation. Two transcription initiation sites (TISs) were ***identified*** in each of three different CD34+ cell lines; these TISs were located at 120 and 80 bp 5' of the translation start site, respectively. The promoter lacks TATA elements and, like other TATA-less promoters, the TISs conform to the consensus sequence for an INR (PyPyCAPyPyPyPy). An additional 3000 bp of upstream genomic DNA were sequenced and found to contain consensus sites for transcription factors, suggesting their potential role in gene regulation. Transient ***transfection*** assays using CD34 promoter-luciferase ***reporter*** constructs, containing sequences up to 3 kb upstream and inclusive of the TIS, indicate that this promoter drives transcription in

hematopoietic CD34+ cells but not CD34+ non-hematopoietic cells. Both cell type-specific expression and full promoter activity are maintained in constructs that contain as little as 454 bp upstream of the TISs. Optimal promoter activity requires the 5' untranslated region of exon 1, which contains a 51-bp element that has the potential to form an extensive secondary structure. In the plasmid DNA, however, this secondary structure was not detectable by P1 nuclease digestion. At least three proteins present in uninduced M1 nuclear extracts bind to this element. Two of the three proteins were ***identified*** as Sp 1 and Sp 3 based on supershift experiments. These data suggest that CD34 expression by hematopoietic stem and progenitor cells involves hematopoietic cell-specific factors that interact with regulatory elements within the first 230 bp of the promoter and that optimal expression requires a 60-bp segment of the 5' untranslated region.

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on STN
AN 97009134 EMBASE
DN 1997009134
TI ***Identification*** of genes induced by factor deprivation in hematopoietic cells undergoing apoptosis using gene-trap mutagenesis and site-specific recombination.
AU Russ A.P.; Friedel C.; Ballas K.; Kalina U.; Zahn D.; Strebhardt K.; Von Melchner H.
CS H. Von Melchner, Laboratory for Molecular Hematology, Department of Hematology, Univ. of Frankfurt Medical School, Theodor-Stern-Kai 7, 60590 Frankfurt am Main, Germany. melchner@em.uni-frankfurt.de
SO Proceedings of the National Academy of Sciences of the United States of America, (1996) 93/28 (15279-15284).
Refs: 38
ISSN: 0027-8424 CODEN: PNASAB
CY United States
DT Journal; Article
FS 029 Clinical Biochemistry
LA English
SL English
AB A strategy employing gene-trap mutagenesis and site-specific recombination (Cre/loxP) has been developed to ***isolate*** genes that are transcriptionally activated during programmed cell death. Interleukin-3 (IL-3) dependent hematopoietic precursor cells (FDCP1) expressing a ***reporter*** plasmid that codes for herpes simplex virus-thymidine kinase, neomycin phosphotransferase, and murine IL-3 were ***transduced*** with a retroviral gene-trap vector carrying coding sequences for Cre-recombinase (Cre) in the U3 region. Activation of Cre expression from integrations into active genes resulted in a permanent switching between the selectable marker genes that converted the FDCP1 cells to factor independence. Selection for autonomous growth yielded recombinants in which Cre sequences in the U3 region were expressed from upstream cellular promoters. Because the expression of the marker genes is independent of the trapped cellular promoter, genes could be ***identified*** that were transiently induced by IL-3 withdrawal.

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on STN
AN 96338274 EMBASE
DN 1996338274
TI Spatial and temporal patterns of c-kit-expressing cells in W(lacZ)/+ and W(lacZ)/W(lacZ) mouse embryos.
AU Bernex F.; De Sepulveda P.; Kress C.; Elbaz C.; Delouis C.; Panthier J.-J.
CS URA-INRA de Genetique Moleculaire, Ecole Nationale Veterinaire d'Alfort, 7 avenue du General-de-Gaulle, 94704 Maisons-Alfort cedex, France
SO Development, (1996) 122/10 (3023-3033).
ISSN: 0950-1991 CODEN: DEVPED
CY United Kingdom
DT Journal; Article
FS 021 Developmental Biology and Teratology
LA English
SL English
AB In the mouse, the Kit receptor and its ligand, the stem cell factor (SCF), are encoded at the W/Kit and Steel loci, respectively. The Kit/SCF ***transduction*** pathway is involved in promoting cellular migration, proliferation and/or survival of melanoblasts, hematopoietic progenitors and primordial germ cells. Furthermore, a functional Kit/SCF pathway is required for the development of interstitial cells of Cajal (ICC) in the small intestine. Whereas all c-kit-expressing cells in embryogenesis were not ***identified***, previous studies clearly demonstrated that the c-kit expression pattern extends well beyond cells known to be affected by W mutations. To investigate further Kit function, we specifically marked the c-kit-expressing cells and followed their fate during embryogenesis. A mutation was introduced by gene targeting at the W/Kit locus in mouse embryonic stem cells. The lacZ ***reporter*** gene was inserted into the first exon of c-kit, thus creating a null allele, called W(lacZ). The lacZ expression reflects normal expression of the c-kit gene in W(lacZ)/+ embryos. The comparison of the patterns of lacZ-expressing cells between W(lacZ)/+ and W(lacZ)/W(lacZ) embryos allowed us to detect where and when melanoblasts, primordial germ cells and hematopoietic progenitors failed to survive in the absence of Kit. We also observed that ICC express c-kit during embryogenesis, ICC are found identically in W(lacZ)/+ and W(lacZ)/W(lacZ) embryos. Therefore, ICC do not depend on Kit expression during embryogenesis. These results indicate that the function of the c-kit gene is only required for the postnatal development of the ICC.

Unexpected sites of c-kit expression were uncovered in embryos, including endothelial, epithelial and endocrine cells. None of these cells are dependent on Kit expression for their migration, proliferation and/or survival during embryogenesis. Nevertheless, we assume that the Kit/SCF pathway could be involved in the growth of ***transformed*** endothelial, epithelial and endocrine cells.

L18 ANSWER 30 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 11
AN 1995:252272 BIOSIS
DN PREV199598266572
TI Activity and expression of murine small Maf family protein MafK.
AU Igarashi, Kazuhiko [Reprint author]; Itoh, Ken [Reprint author]; Motohashi, Hozumi [Reprint author]; Hayashi, Norio [Reprint author]; Matuzaki, Yumi; Nakauchi, Hiromitsu; Nishizawa, Makoto; Yamamoto, Masayuki [Reprint author]
CS Dep. Biochem., Tohoku Univ. Sch. Medicine, 2-1 Seiryomachi, Aoba-ku, Sendai 980-77, Japan
SO Journal of Biological Chemistry, (1995) Vol. 270, No. 13, pp. 7615-7624.
CODEN: JBCHA3. ISSN: 0021-9258.
DT Article
LA English
OS EMBL-D42124; Genbank-D42124
ED Entered STN: 13 Jun 1995
Last Updated on STN: 13 Jun 1995

AB Transcription factor NF-E2 is believed to be crucial for the regulation of erythroid-specific gene transcription. The three small Maf family proteins (MafF, MafG, and MafK), which are closely related to c-Maf protooncoprotein, constitute half of NF-E2 activity by virtue of forming heterodimers with the large, tissue-restricted subunit of NF-E2 (p45). We ***isolated*** cDNA clones encoding the murine small Maf family protein MafK and characterized the structure, activity, and expression profile of MafK mRNA. Functional analyses demonstrate that MafK binds to consensus NF-E2 sites in the absence of p45 in vitro and represses transcription of NF-E2 site-dependent ***reporter*** genes in transient ***transfection*** assays, while p45 introduced into cells alone does not effectively bind to DNA and does not affect transcription. In the presence of p45, MafK confers site-specific DNA binding activity to p45, and p45 in turn mediates transcriptional activation with its amino-terminal proline-rich domain. mRNA for MafK is expressed in fractions enriched for ***hematopoietic*** ***stem*** ***cells*** as well as erythroid cells, suggesting that MafK plays an important regulatory role in hematopoiesis.

L18 ANSWER 31 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 12
AN 1995:387504 BIOSIS
DN PREV199598401804
TI Myeloproliferative sarcoma virus directed expression of beta-galactosidase following retroviral ***transduction*** of murine hematopoietic cells.
AU Clapp, D. Wade [Reprint author]; Freie, Brian; Strout, Edward; Yoder, Mervin C.; Fortney, Kate; Gerson, S. L.
CS Herman B. Wells Res. Cent., 702 Barnhill Drive, RR 208, Indianapolis, IN 46202, USA
SO Experimental Hematology (Charlottesville), (1995) Vol. 23, No. 7, pp. 630-638.
CODEN: EXHMA6. ISSN: 0301-472X.
DT Article
LA English
ED Entered STN: 13 Sep 1995
Last Updated on STN: 13 Sep 1995

AB The introduction of genetic sequences into ***hematopoietic*** ***stem*** ***cells*** (HSC) has allowed study of HSC proliferation in vivo by proviral-sequence molecular analysis in the DNA of progeny. Analysis of HSC proliferation could be enhanced by development of a retroviral vector that encodes a ***reporter*** gene that allows sensitive detection of ***transduced*** cells. We developed a recombinant retrovirus vector encoding the ***reporter*** gene lacZ under the transcriptional control of the myeloproliferative sarcoma virus long-terminal repeat (LTR). Bone marrow cells from C3H mice were co-cultured on retrovirus producer cell lines and cultured for growth of colony-forming unit granulocyte/macrophage (CFU-GM) and high proliferative potential colony-forming cells (HPP-CFC) in semisolid media or were transplanted into irradiated recipients. In other experiments, recombinant retrovirus was injected in vivo into the liver of developing fetal rat pups, and circulating hematopoietic cells of the postnatal rats were analyzed for evidence of proviral integration and expression of beta-galactosidase. Expression of lacZ was detected in both CFU-GM and HPP-CFC that were cultured immediately following in vitro infection of mouse bone marrow. beta-galactosidase activity from the retrovirus was also detected in bone marrow cells ***isolated*** from reconstituted mice 22 weeks following transplantation as well as in blood cells of postnatal rats ***transduced*** in utero with the recombinant retrovirus. This strategy may be especially useful for characterizing proliferation of ***transduced*** populations of hematopoietic cells and in the development of protocols for somatic gene therapy.

L18 ANSWER 32 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 13
AN 1994:28983 BIOSIS

DN PREV199497041983

TI Molecular regulation of the human IL-3 gene: Inducible T cell-restricted expression requires intact AP-1 and E1f-1 nuclear protein binding sites.

AU Gottschalk, Lisa R. [Reprint author]; Giannola, Diane M.; Emerson, Stephen G.

CS Dep. Med., Univ. Chicago, 5841 S. Maryland, MC5041, Chicago, IL 60637, USA

SO Journal of Experimental Medicine, (1993) Vol. 178, No. 5, pp. 1681-1692.

CODEN: JEMEAU. ISSN: 0022-1007.

DT Article

LA English

ED Entered STN: 27 Jan 1994

Last Updated on STN: 27 Jan 1994

AB Interleukin 3 (IL-3) is a ***hematopoietic*** ***stem*** - ***cell*** growth and differentiation factor that is expressed solely in activated T and NK cells. Studies to date have ***identified*** elements 5' to the IL-3 coding sequences that regulate its transcription, but the sequences that confer T cell-specific expression remain to be clearly defined. We have now ***identified*** DNA sequences that are required for T cell-restricted IL-3 gene transcription. A series of transient ***transfections*** performed with human IL-3-chloramphenicol acetyltransferase (CAT) ***reporter*** plasmids in T and non-T cells revealed that a plasmid containing 319 bp of 5' flanking sequences was active exclusively in T cells. Deletion analysis revealed that T cell specificity was conferred by a 49-bp fragment (bp -319 to -270) that included a potential binding site for AP-1 transcription factors 6 bp upstream of a binding site for E1f-1, a member of the Ets family of transcription factors. DNase1 footprint and electrophoretic mobility shift assay analyses performed with MLA-144 T cell nuclear extracts demonstrated that this 49-bp region contains a nuclear protein binding region that includes consensus AP-1 and E1f-1 binding sites. In addition, extracts prepared from purified human T cells contained proteins that bound to synthetic oligonucleotides corresponding to the AP-1 and E1f-1 binding sites. In vitro-transcribed and -translated E1f-1 protein bound specifically to the E1f-1 site, and E1f-1 antisera competed and super shifted nuclear protein complexes present in MLA-144 nuclear extracts. Moreover, addition of anti-Jun family antiserum in electrophoretic mobility shift assay reactions completely blocked formation of the AP-1-related complexes. Transient ***transfection*** studies in MLA-144 T cells revealed that constructs containing mutations in the AP-1 site almost completely abolished CAT activity while mutation of the E1f-1 site or the NF-IL-3 site, a previously described nuclear protein binding site (bp -155 to -148) in the IL-3 promoter, reduced CAT activity to 1/25 of the activity given by wild-type constructs. We conclude that expression of the human IL-3 gene requires the AP-1 and E1f-1 binding sites; however, unlike other previously characterized cytokine genes such as IL-2, the AP-1 and E1f-1 factors can bind independently in the IL-3 gene. Thus, the exact DNA composition of these sites, flanking DNA sequences, and the distance between the AP-1 and Ets family binding sites determine the fine specificity of nuclear factors that bind to these sites and the resulting inducible, cell-restricted expression of a group of lymphokine genes.

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FULL ESTIMATED COST 2.45 191.64

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L3	5 DUP REM L2 (0 DUPLICATES REMOVED)
L4	29844 S HEMATOPOI? STEM CELL?
L5	529 S L4 (5A) (ISOLAT? OR IDENTIF? OR SORT?)
L6	0 S L5 AND REPORTER AND GENOMIC LOC?
L7	4 S L5 AND REPORTER
L8	67 S L5 AND MARKER
L9	116 S L5 AND MARKER?
L10	4 DUP REM L7 (0 DUPLICATES REMOVED)
L11	1 S L9 AND IKAROS
L12	1 S L9 AND SCL
L13	6 S L5 AND (IKAROS OR SCL)
L14	3 DUP REM L13 (3 DUPLICATES REMOVED)
L15	4631 S L4 AND (TRANSDUC? OR TRANSFEC? OR TRANSFOR?)
L16	202 S L15 AND REPORTER
L17	56 S L16 AND (IDENTIF? OR ISOLAT?)
L18	32 DUP REM L17 (24 DUPLICATES REMOVED)
L19	0 S L18 AND GENOMIC LOC?

FILE 'STNGUIDE' ENTERED AT 16:20:49 ON 12 FEB 2004

FILE 'BIOSIS, MEDLINE, EMBASE' ENTERED AT 16:33:28 ON 12 FEB 2004

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 16:33:31 ON 12 FEB 2004

=> s l4 and ikaros

L20 60 L4 AND IKAROS

=> s l4 and scl

L21 140 L4 AND SCL

=> s l20 and loci

L22 3 L20 AND LOCI

=> dup rem l22

PROCESSING COMPLETED FOR L22

L23 3 DUP REM L22 (0 DUPLICATES REMOVED)

=> d bib abs 1-

YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):y

L23 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS ON STN

AN 2002:637806 CAPLUS

DN 137:152031

TI Stem cell self-renewal and lineage commitment

IN Chan, Chang-zheng; Lodish, Harvey F.

PA Whithead Institute for Biomedical Research, USA

SO PCT Int. Appl., 36 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2002064756	A2	20020822	WO 2002-US4459	20020215
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WO 2002064756	C2	20021114		
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WO 2002064756	A3	20030109		
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WO 2002064756	C1	20030410		
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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002168660 A1 20021114 US 2002-77178 20020215
PRAI US 2001-269060P P 20010215
AB Methods of marking pluripotent cells, such as stem cells, particularly
hematopoietic ***stem*** ***cells*** ; methods of
detecting/identifying, enriching, selecting and monitoring pluripotent
cells (stem cells); DNA constructs useful in the methods; stem cells, such
as ***hematopoietic*** ***stem*** ***cells***, identified by
the method; as well as lineage-specific cells identified by the method;
and uses for the cells are subjects of this invention. The cells are
marked by targeting reporter genes into ***loci*** that are
functionally specific and important for ***hematopoietic***
stem ***cell*** activity (e.g., self-renewal or lineage
commitment). Combinations of targeted markers are used to provide phys.
and functional identities for the cells. Two ***loci***, stem cell
leukemia (SCL) and ***ikaros***, were targeted using HuCD4/RES/puro
and .beta.neo(lacZneo) reporter cassettes, resp.

L23 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS
INC. on STN
AN 2001:312497 BIOSIS
DN PREV200100312497
TI ***ikaros*** is required for the formation and function of an
hematopoietic cell-specific chromatin remodeling complex.
AU Lopez, Rocio L. [Reprint author]; Schoetz, Stuti S. [Reprint author];
Georgopoulos, Katia; O'Neill, David W.; Bank, Arthur [Reprint author]
CS Genetics and Development, Columbia University, New York, NY, USA
SO Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 497a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology.
San Francisco, California, USA, December 01-05, 2000. American Society of
Hematology.
CODEN: BLOODAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 27 Jun 2001
Last Updated on STN: 19 Feb 2002
AB We have recently characterized an hematopoietic cell-specific chromatin
remodeling complex (PYR complex) from mouse erythroleukemia (MEL) cells
that binds long polypyrimidine sequences in the mouse and human
beta-globin ***loci*** (O'Neill et al, MCB, in press). PYR complex
contains the hematopoietic cell-specific DNA binding protein
ikaros together with both activator (SWI/SNF) and repressor (NuRD,
histone deacetylase and Mi-2) chromatin-remodeling subunits. In purifying
PYR complex from MEL nuclear extract by chromatography, we only find
ikaros in fractions that contain PYR complex DNA-binding activity.
This suggests that ***ikaros*** is always associated with chromatin
remodeling subunits in PYR complex. To further explore the role of
ikaros in PYR complex in vivo, we looked for PYR complex
DNA-binding activity in the hematopoietic tissues of mice with a targeted
null mutation in the ***ikaros*** gene (***ikaros*** null mice)
that have no detectable ***ikaros*** RNA or protein. PYR DNA-binding
activity is absent in homozygous (-/-) null mice, indicating that PYR
complex requires ***ikaros*** to bind DNA in vivo. In addition, PYR
complex is reduced to about 50% of control amounts in heterozygous (+/-)
mice, showing that the amount of PYR complex is proportional to the amount
of ***ikaros*** in vivo. ***ikaros*** -/- mice have previously
been shown to have severe defects in lymphocyte development and decreased
hematopoietic ***stem*** ***cell*** activity. We now find
that they also have a moderate anemia, aniso- and poikilocytosis, an
elevated reticulocyte count, a 3- to 4-fold increase in the platelet
count, and myeloid metaplasia in the spleen. These data are consistent
with an in vivo role for PYR complex in all hematopoietic lineages as
suggested by our previous findings that ***ikaros*** and PYR complex
are normally present in adult erythroid, myeloid, megakaryocytic and T and
B cell lines, and absent in non-hematopoietic tissues. Taken together
with our observation that all of ***ikaros*** is associated with
chromatin remodeling factors in PYR complex, it is likely that the
multiple hematopoietic cell defects found in ***ikaros*** null mice
are due to impaired targeting of PYR complex to specific DNA sequences in
adult hematopoietic lineages.

L23 ANSWER 3 OF 3 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL
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on STN
AN 2000231287 EMBASE
TI Transcriptional regulation of early B-lymphocyte differentiation.
AU O'Riordan M.; Grosschedl R.
CS R. Grosschedl, Gene Center/Department Biochemistry, University of Munich,
Feodor Lynen Str. 25, 81377 Munich, Germany. rgross@lmb.uni-muenchen.de
SO Immunological Reviews, (2000) 175/- (94-103).
Refs: 103
ISSN: 0105-2898 CODEN: IMRED2
CY Denmark
DT Journal; Article
FS 022 Human Genetics
026 Immunology, Serology and Transplantation
LA English
SL English
AB Differentiation of hematopoietic progenitors into the B-lymphocyte lineage
requires co-ordination of a complex network of transcriptional regulators.
Lineage specificity is likely to result from combinatorial mechanisms of
gene regulation. Four general functions are mediated by transcription
factors in the differentiating pro-B cell. First, a cascade of

B-cell-restricted transcription factors is upregulated. Second, genes
involved in the specification of other cell fates are repressed. Both
activation and repression require the participation of different classes
of transcriptional regulators, including proteins of the ***ikaros***
family that can recruit chromatin-modifying complexes. Third, the
expression of genes that facilitate B-cell proliferation and
differentiation are activated. Lastly, genes required for recombination
are expressed and targeted to the immunoglobulin ***loci***, thus
initiating the characteristic rearrangement of the immunoglobulin genes.
The interactions and functions of transcription factors in pro-B-cell
differentiation are discussed.

=> s l21 and loci
L24 4 L21 AND LOCI

=> dup rem l24
PROCESSING COMPLETED FOR L24
L25 3 DUP REM L24 (1 DUPLICATE REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):y

L25 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:35358 CAPLUS
TI ***SCL*** : From the origin of hematopoiesis to stem cells and leukemia
AU Lecuyer, Eric; Hoang, Trang
CS and Molecular Biology, Biochemistry, Canada; Departments of Pharmacology,
Quebec, Montreal, Institut de Recherche en Immunovirologie et Cancerologie
(IRIC), Université de Montreal, Montreal, QC, Can.
SO Experimental Hematology (New York, NY, United States) (2004), 32(1), 11-24
CODEN: EXHMA6; ISSN: 0301-472X
PB Elsevier Science Inc.
DT Journal
LA English
AB In the hematopoietic system, lineage commitment and differentiation is
controlled by the combinatorial action of transcription factors from
diverse families. ***SCL*** is a basic helix-loop-helix transcription
factor that is an essential regulator at several levels in the
hematopoietic hierarchy and whose inappropriate regulation frequently
contributes to the development of pediatric T-cell acute lymphoblastic
leukemia. This review discusses advances that have shed important light
on the functions played by ***SCL*** during normal hematopoiesis and
leukemogenesis and have revealed an unexpected robustness of
hematopoietic ***stem*** ***cell*** function. Mol.
studies have unraveled a mechanism through which gene expression is
tightly controlled, as ***SCL*** functions within multifactorial
complexes that exhibit an all-or-none switch-like behavior in
transcription activation, arguing for a quantal process that depends on
the concurrent occupation of target ***loci*** by all members of the
complex. Finally, variations in compn. of ***SCL*** -contg. complexes
may ensure flexibility and specificity in the regulation of
lineage-specific programs of gene expression, thus providing the mol.
basis through which ***SCL*** exerts its essential functions at
several branch points of the hematopoietic hierarchy.

L25 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:637806 CAPLUS
DN 137:152031
TI Stem cell self-renewal and lineage commitment
IN Chan, Chang-zheng; Lodish, Harvey F.
PA Whithead Institute for Biomedical Research, USA
SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE
PI WO 2002064756 A2 20020822 WO 2002-US4459 20020215
WO 2002064756 C2 20021114
WO 2002064756 A3 20030109
WO 2002064756 C1 20030410
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2002168660 A1 20021114 US 2002-77178 20020215
PRAI US 2001-269060P P 20010215
AB Methods of marking pluripotent cells, such as stem cells, particularly
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detecting/identifying, enriching, selecting and monitoring pluripotent
cells (stem cells); DNA constructs useful in the methods; stem cells, such
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the method; as well as lineage-specific cells identified by the method;
and uses for the cells are subjects of this invention. The cells are
marked by targeting reporter genes into ***loci*** that are

functionally specific and important for ***hematopoietic***
stem ***cell*** activity (e.g., self-renewal or lineage
commitment). Combinations of targeted markers are used to provide phys.
and functional identities for the cells. Two ***loci***, stem cell
leukemia (***SCL***) and Ikaros, were targeted using HuCD4/RES/puro
and .beta.neo(lacZneo) reporter cassettes, resp.

L25 ANSWER 3 OF 3 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL
RIGHTS RESERVED.

on STN DUPLICATE 1

AN 1998418902 EMBASE

TI Recent progress in identifying genes regulating ***hematopoietic***
stem ***cell*** function and fate.

AU Jordan C.T.; Van Zant G.

CS C.T. Jordan, Blood Marrow Transplantation Program, Markey Cancer Center,
University Kentucky Medical Center, 800 Rose Street, Lexington, KY 40536,
United States. cjordan@pop.uky.edu

SO Current Opinion in Cell Biology, (1998) 10/6 (716-720).

Refs: 46

ISSN: 0955-0674 CODEN: COCBE3

CY United Kingdom

DT Journal; General Review

FS 021 Developmental Biology and Teratology

025 Hematology

029 Clinical Biochemistry

LA English

SL English

AB Significant advances in the use of genetic and molecular biology
strategies have recently begun to identify genes that have a major impact
on the determination, commitment and developmental potential of
hematopoietic ***stem*** ***cells***. Using a variety of
experimental strategies, genes such as ***SCL***, GATA-2, HoxB4,
Flk-2, c-mpl, dlk, and others have been implicated as important regulators
of stem cell growth. In addition, genetic mapping has identified several
loci that correlate strongly with stem cell numbers and
proliferation.

=>

---Logging off of STN---

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Executing the logoff script...

=> LOG Y

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	ENTRY	SINCE FILE SESSION
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STN INTERNATIONAL LOGOFF AT 16:38:28 ON 12 FEB 2004